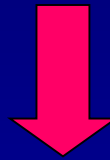
# La Neurochirurgia Funzionale

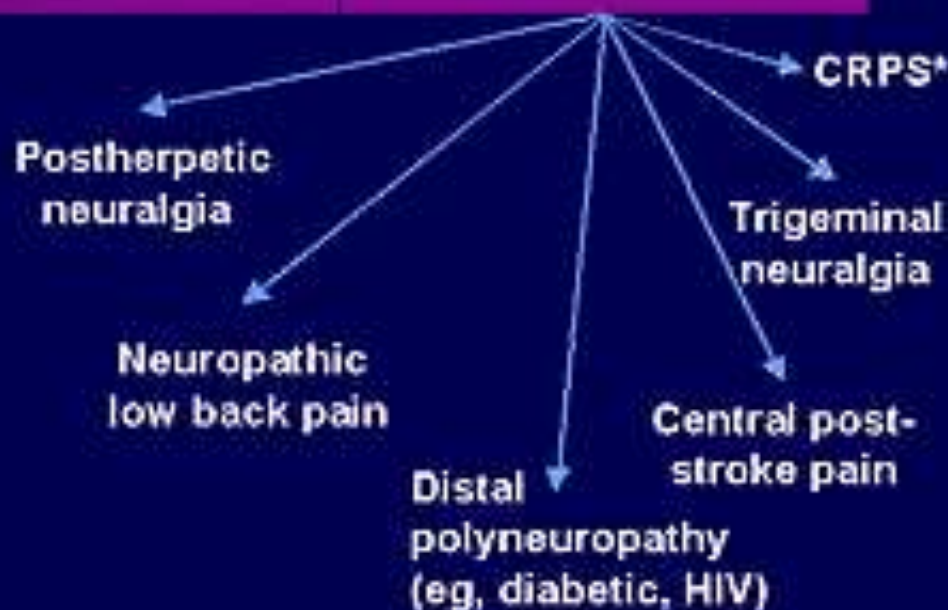
- ❖ cerca di ripristinare una funzione neurologica perduta o alterata
- ❖ è una chirurgia elettiva

**Il deterioramento neurologico intraoperatorio è inaccettabile**

La Neurofisiologia intraoperatoria permette di:

- Riconoscere le strutture target
- Controllare il rischio di complicanze a carico di strutture nervose limitrofe
- Documentare l'appropriatezza dell'intervento chirurgico
- Suggerire i meccanismi di azione del trattamento stesso

# Trattamento chirurgico del dolore neuropatico

# Nociceptive vs Neuropathic Pain

| Nociceptive Pain | Mixed Type | Neuropathic Pain |
| --- | --- | --- |
| Caused by activity in neural pathways in response to potentially tissue-damaging stimuli | Caused by a combination of both primary injury or secondary effects | Initiated or caused by primary lesion or dysfunction in the nervous system |

*Complex regional pain syndrome

# Neuropathic Pain: Issues and Challenges

- Common type of pain
  - 25% to 50% of all pain clinic visits
- Underassessment and undertreatment
- Interpatient variability in response to treatment
- Patient not believed
- Complex pathophysiology

# Potential Descriptions of Neuropathic Pain

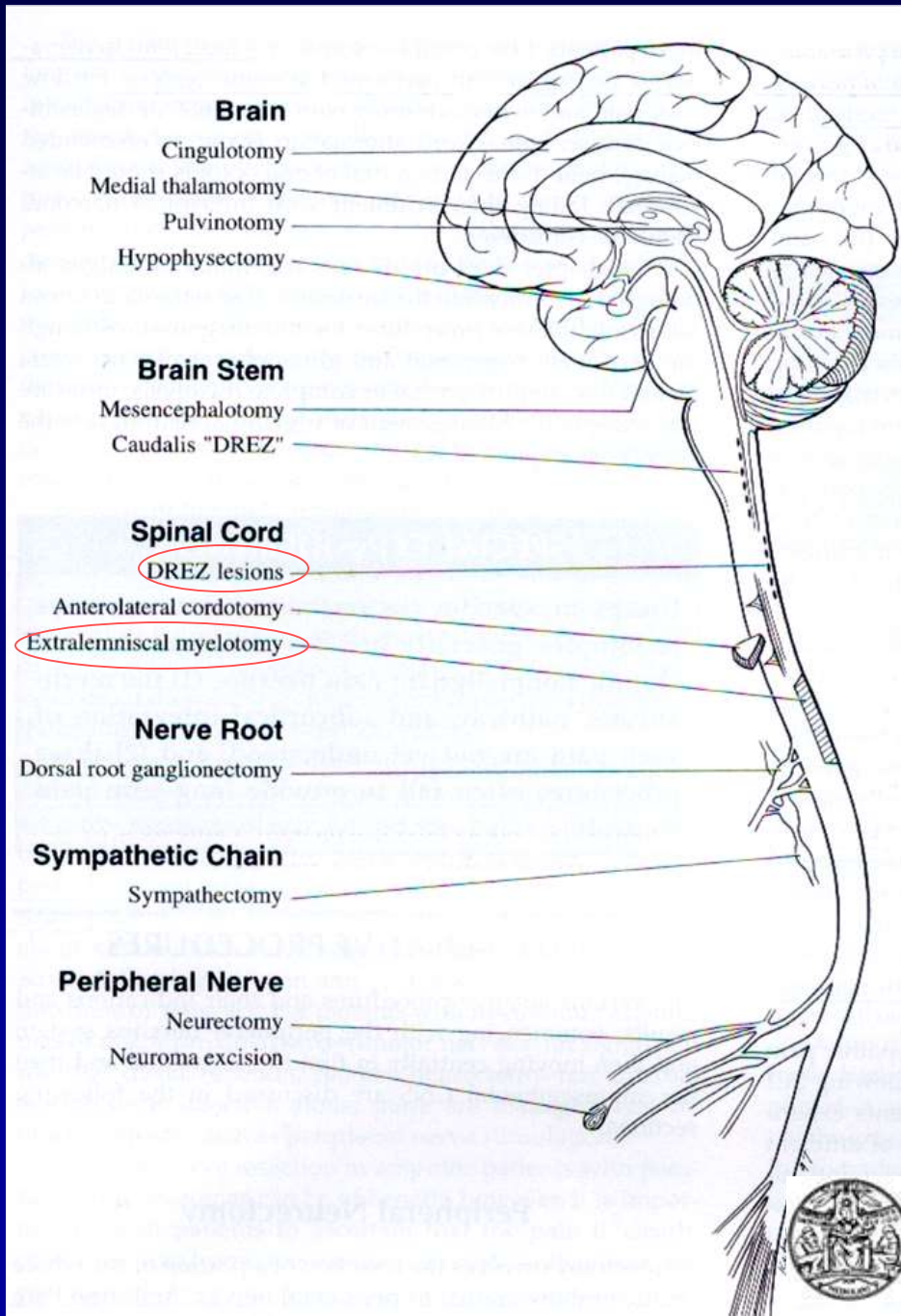
- Sensations
  - burning
  - paresthesia
  - paroxysmal
  - lancinating
  - electriclike
  - raw skin
  - shooting
  - deep, dull, bonelike ache
- Cardinal signs/symptoms
  - allodynia: pain from a stimulus that does not normally evoke pain
    - thermal
    - mechanical
  - hyperalgesia: exaggerated response to a normally painful stimulus

# Dolore cronico benigno:
# il razionale della terapia chirurgica

*INTERVENTI DEMOLITIVI:*

**interrompono le vie di trasmissione del dolore; irreversibili**

- lesione della DREZ

(Sindou, 1974; Nashold, 1976)

# Dolore cronico benigno:
# i limiti della chirurgia demolitiva

- Rischio di danneggiare strutture non coinvolte nella genesi del dolore
- Rischio di provocare effetti collaterali: anestesia dolorosa
- Rischio di recidiva del dolore
- Irreversibilità

# Rilevanza del monitoraggio neurofisiologico intraoperatorio in Neurochirurgia Funzionale

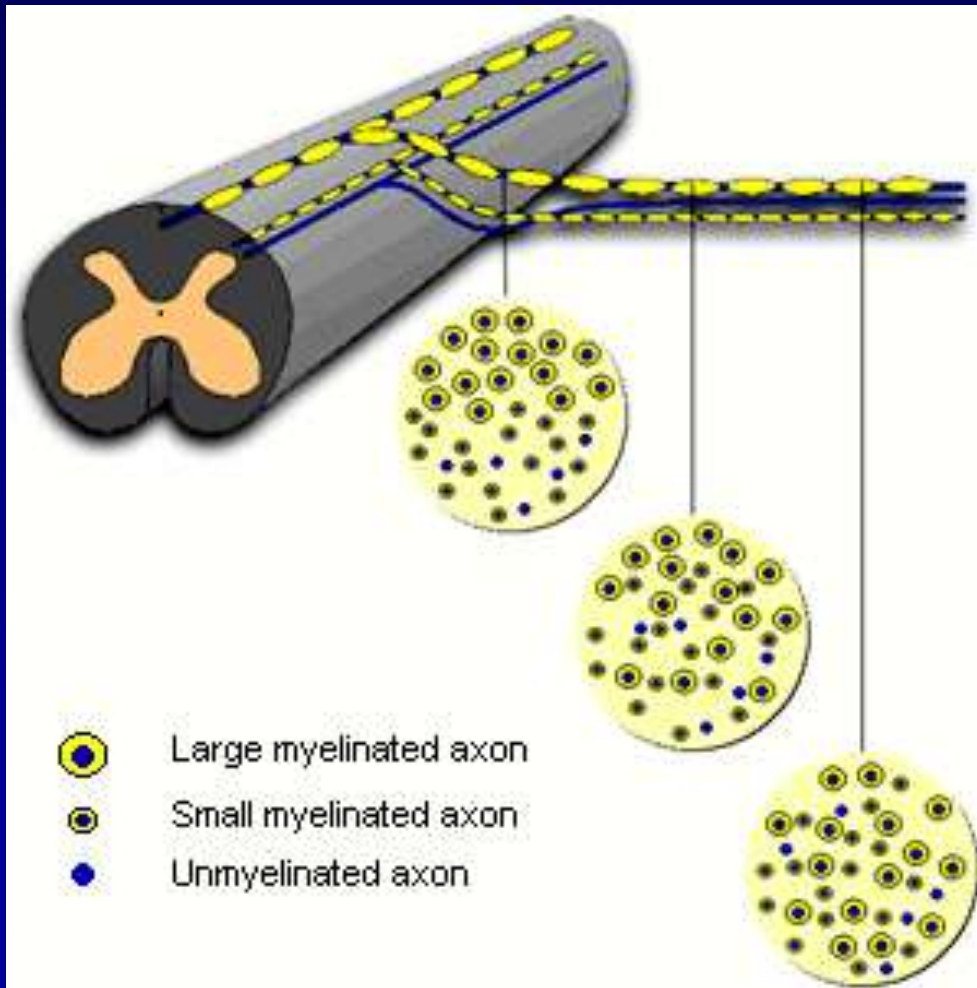
## Lesione della DREZ - Indicazioni

1. dolore da avulsione del plesso o delle radici cervicali
2. nevralgia post-herpetica
3. dolore del paraplegico

1. dolore urente
2. associato a disestesie folgoranti
3. confinato in pochi dermatomeri

# Rilevanza del monitoraggio neurofisiologico intraoperatorio in Neurochirurgia Funzionale

## Lesione della DREZ

Large myelinated axon
Small myelinated axon
Unmyelinated axon

**Distruzione di**:

- parte ventrolaterale delle radici posteriori
- parte mediale del tratto di Lissauer
- lamine più superficiali del corno posteriore

**Per mezzo di:**

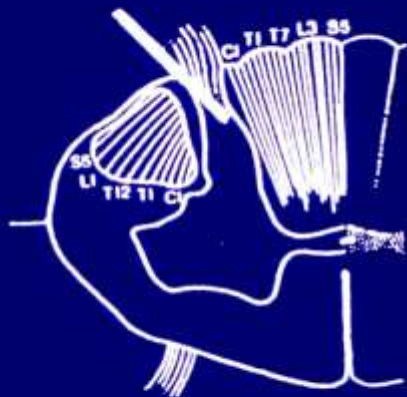
- Microbisturi (Sindou)
- Radiofrequenza (Nashold)
- Laser (Young)

# Rilevanza del monitoraggio neurofisiologico intraoperatorio in Neurochirurgia Funzionale

## Lesione della DREZ - Risultati

| *Autore* | *# pz* | *eccell/buoni* |
|---|---|---|
| Thomas DG, 1994 | 62 | 88% |
| Sindou M, 1995 | 355 | 85% |
| Simpson JM, 1995 | 39 | 74% |
| Rath SA, 1996 | 51 | 45% |
| Samii M, 2001 | 47 | 63% |
| Falci S, 2002 | 32 | 88% |
| Sindou M, 2005 | 44 | 66% |

# Rilevanza del monitoraggio neurofisiologico intraoperatorio in Neurochirurgia Funzionale

## Lesione della DREZ - Complicanze

| *Autore* | *Def. motorio* | *Atassia* |
|---|---|---|
| •Gorecki L, 1995 | 90% | 38% |
| •Rath SA, 1996 | 13% | |
| •Samii M, 2001 | 15% | |
| •Falci S, 2002 | 4% | 17% |
| •Thomas DG, 1994 | 16% | |
| • Sindou M, 2005 | 3.6% | 3.6% |

# LESIONE DELLA DREZ

## *IOM:*

- **PES segmentari (radici e lamine superficiali cor-no posteriore)**
- PES di conduzione (cordoni posteriori)
- PEM onda D (tratto cortico-spinale)

**CASO #1**

E' il caso di un paziente con lesione del plesso brachiale dovuta ad un neurofibroma. Lamentava un dolore neurogeno al braccio e alla mano sinistra. I potenziali evocati somatosensoriali segmentari registrati all'inizio dell'intervento (1Hz-5KHz, N=50-100) presentavano una latenza aumentata (N13 a 18ms), una ampiezza ridotta (5uv) e una durata prolungata (fino a 40 ms). Dopo lesione della DREZ a C6-7 la N13 mostrava una riduzione di ampiezza.

# LESIONE DELLA DREZ

## *IOM:*

- PES segmentari (radici e lamine superficiali corno posteriore)
- **PES di conduzione (cordoni posteriori)**
- PEM onda D (tratto cortico-spinale)

DREZL

Posterior column monitoring

Recording: Stimulation:

I potenziali somatosensoriali di conduzione erano rappresentati da una serie di onde polifasiche con latenza 30ms e durata 10ms. Non vi erano variazioni durante l'intervento.

# LESIONE DELLA DREZ

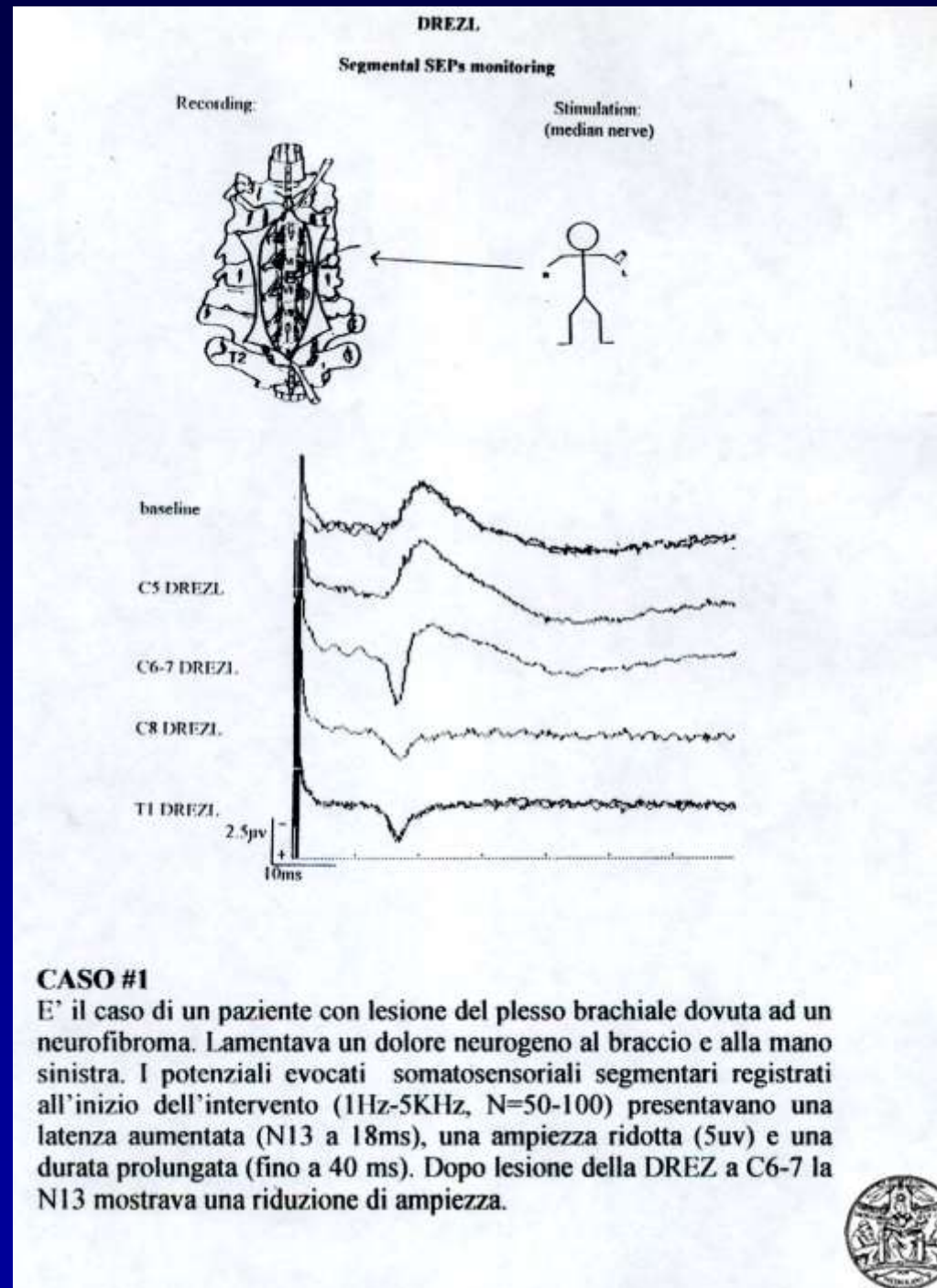
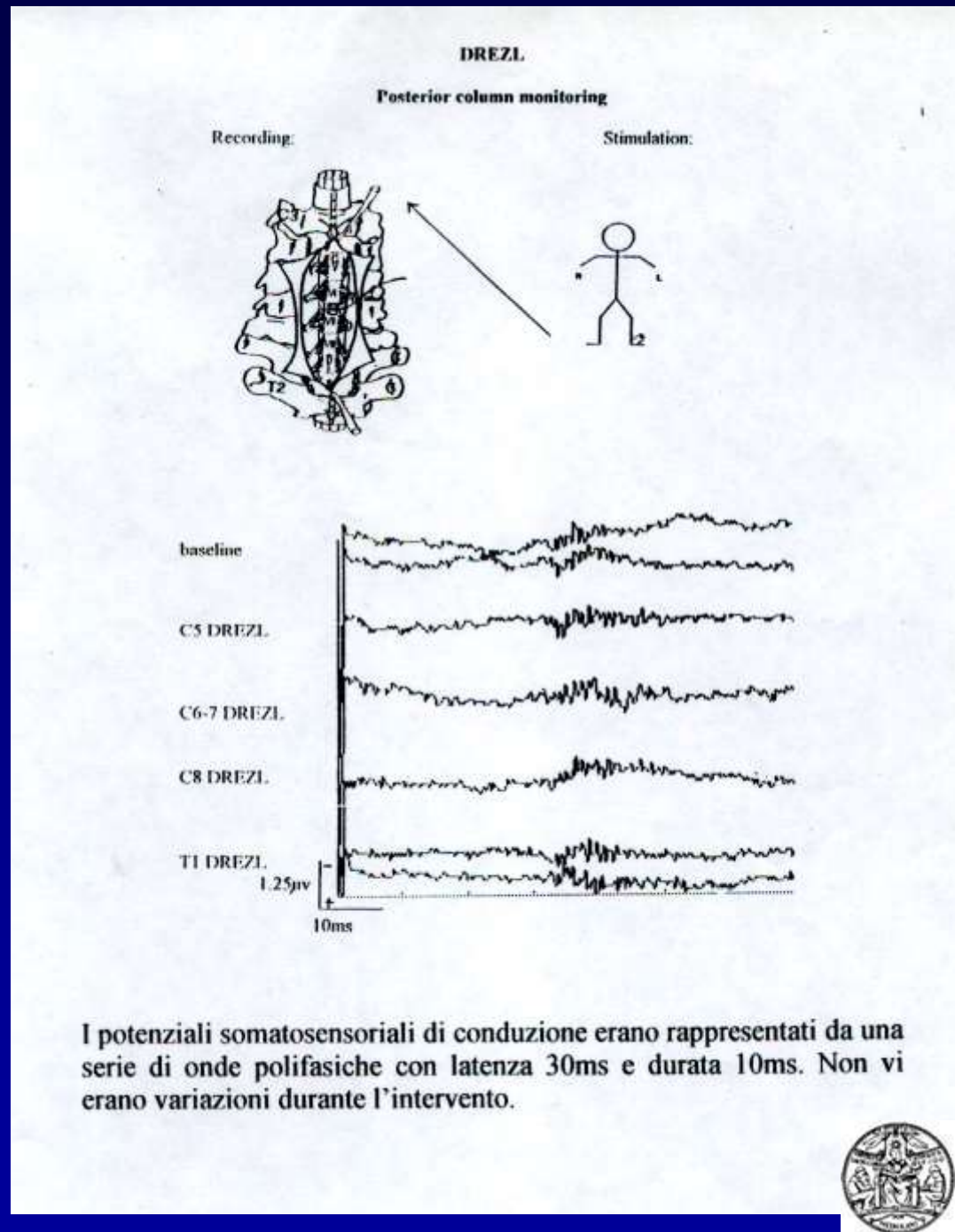
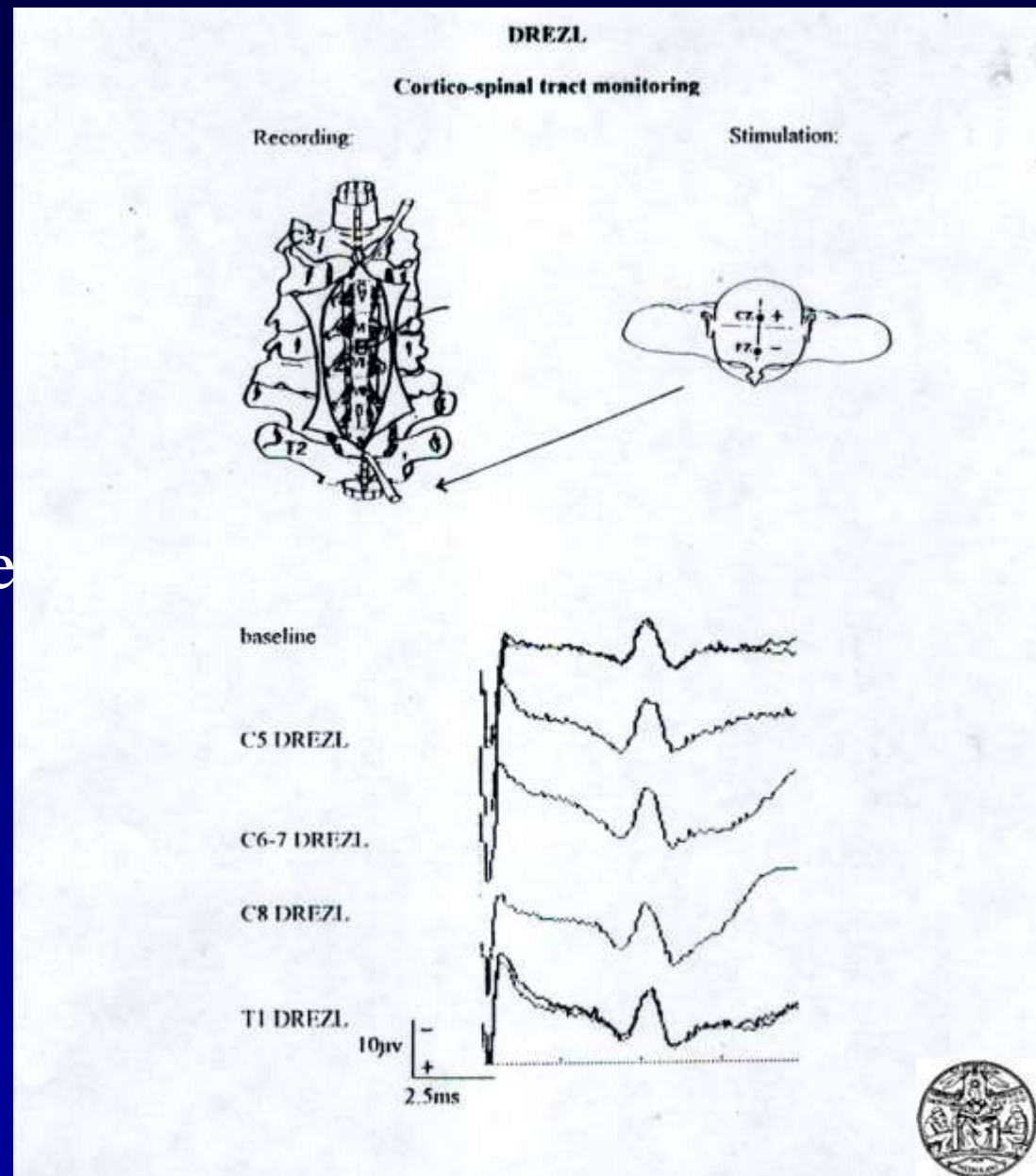
## *IOM:*

•PES segmentari (radici e lamine superficiali corno posteriore)

•PES di conduzione (cordoni posteriori)

**•PEM onda D (tratto cortico-spinale)**

DREZL

Cortico-spinal tract monitoring

L'onda D da attivazione del fascio cortico-spinale aveva latenza 5.5ms ed ampiezza 8uv. Il potenziale era stabile durante tutto il corso dell'intervento.

# Dolore cronico benigno:
# il razionale della terapia chirurgica

*NEUROMODULAZIONE:*

**Interazione reversibile con il funzionamento del sistema nervoso per modularne funzioni alterate o per modificare funzioni di altri organi o apparati.**

-stimolazione elettrica

-applicazione intratecale di farmaci

*NEUROMODULAZIONE:*

•Stimolazione dei nervi periferici

• **Stimolazione del midollo spinale**

• Stimolazione del cervello:
grigia periacqueduttale
e periventricolare
talamo specifico

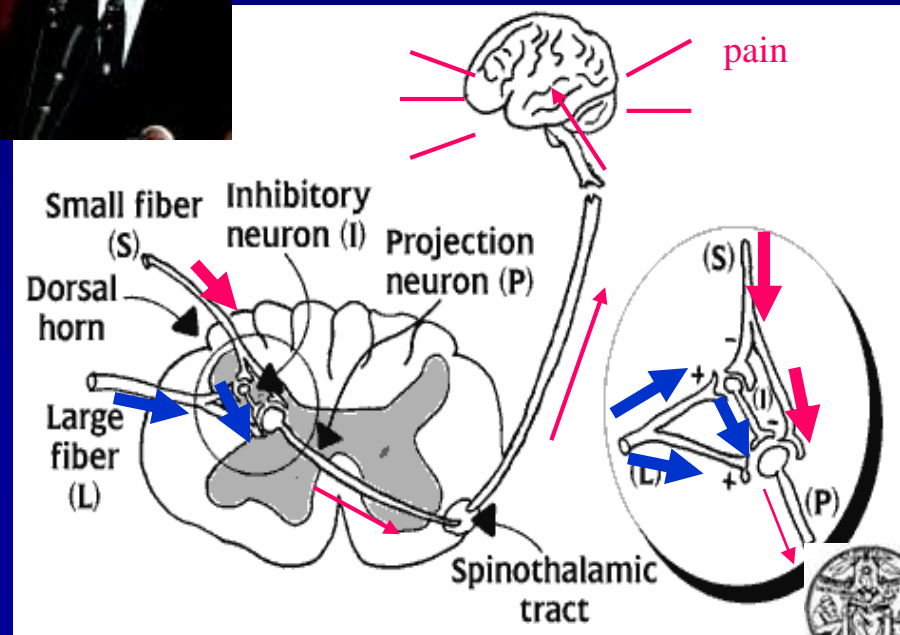
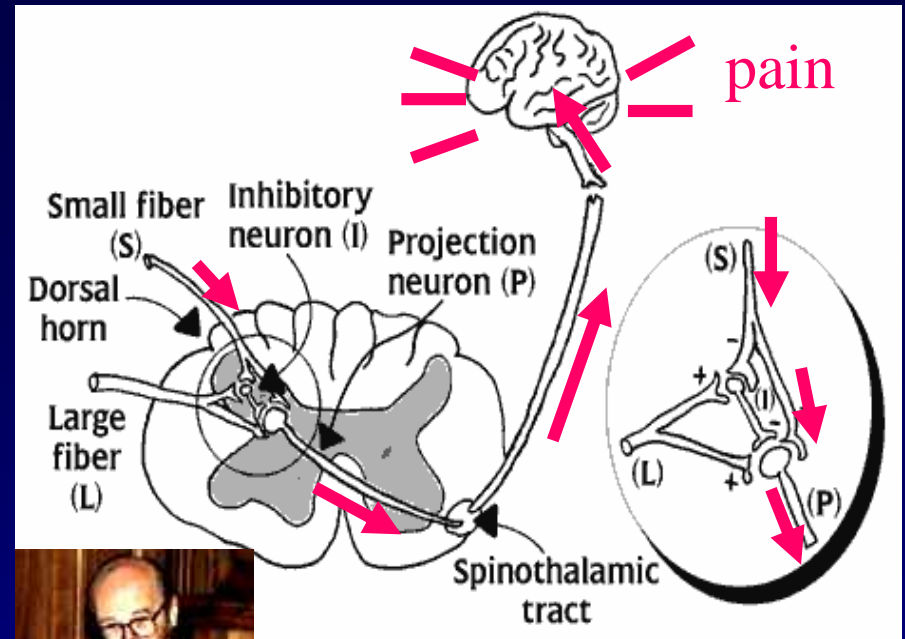
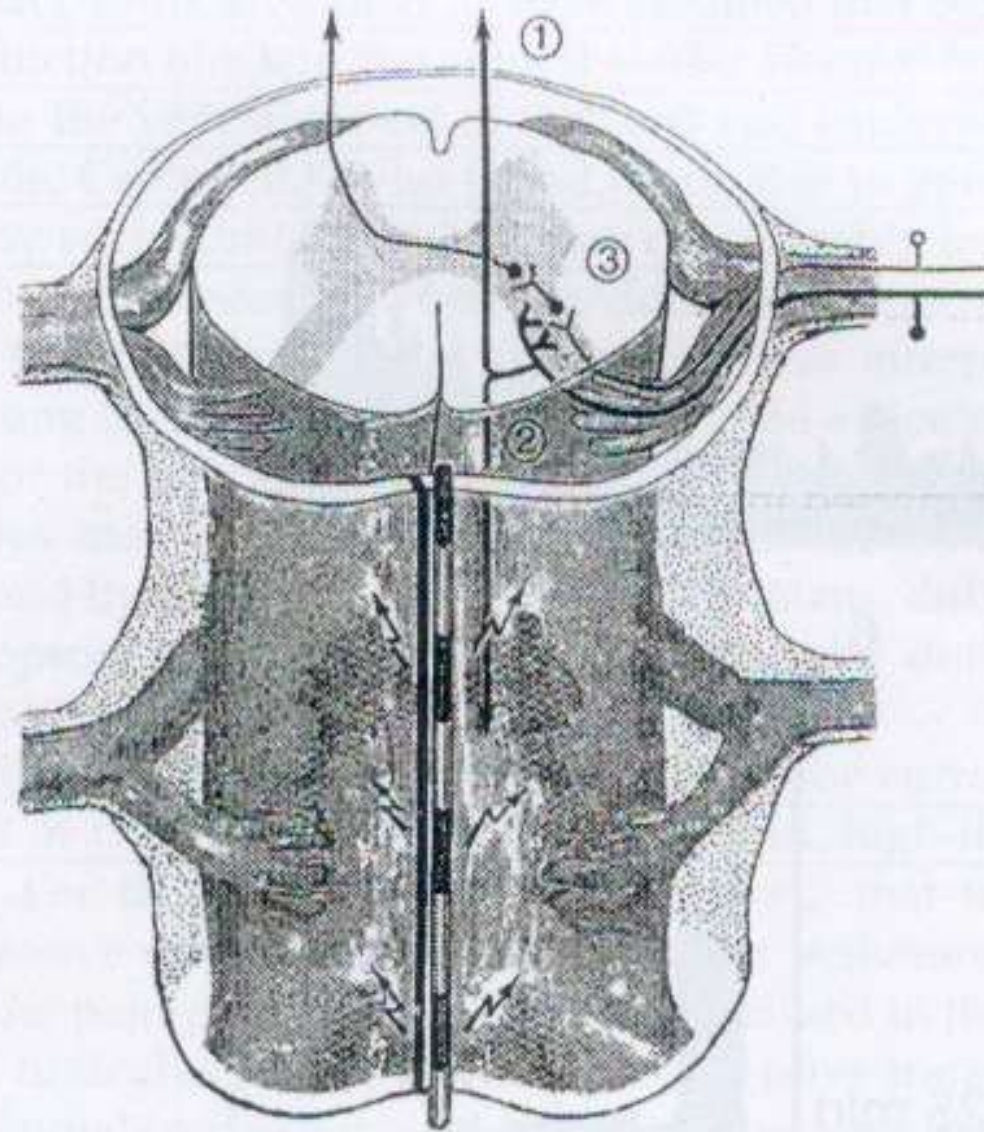
• **Stimolazione della corteccia motoria**

•Applicazione intratecale di farmaci

# TEORIA DEL CANCELLO

**(Melzack e Wall)**

**E’ su questa teoria che si è sviluppata la stimolazione midollare terapeutica**

(Shealy, 1969)

pain

Small fiber (S)

Inhibitory neuron (I)

Projection neuron (P)

Dorsal horn

Large fiber (L)

Spinothalamic tract

pain

Small fiber (S)

Inhibitory neuron (I)

Projection neuron (P)

Dorsal horn

Large fiber (L)

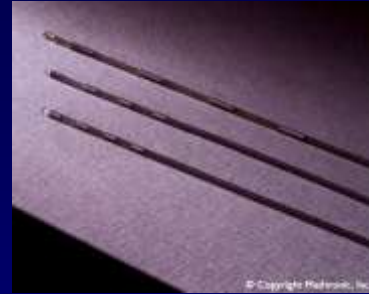
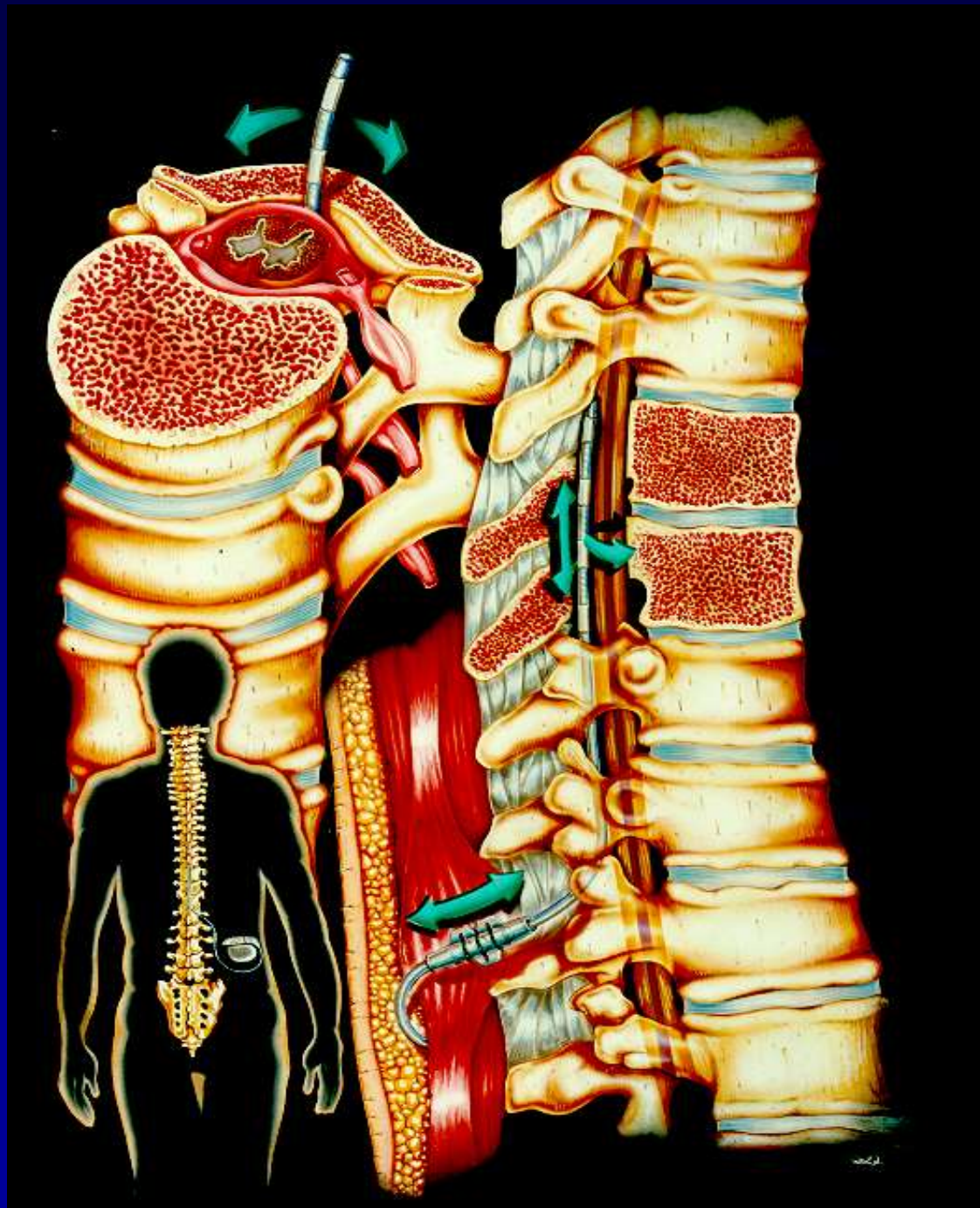
Spinothalamic tract

# La stimolazione del midollo spinale

## TECNICA

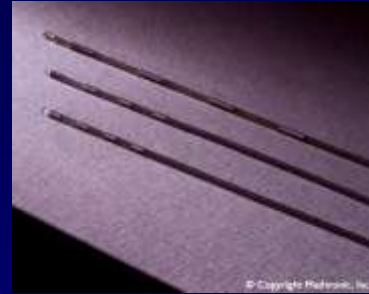
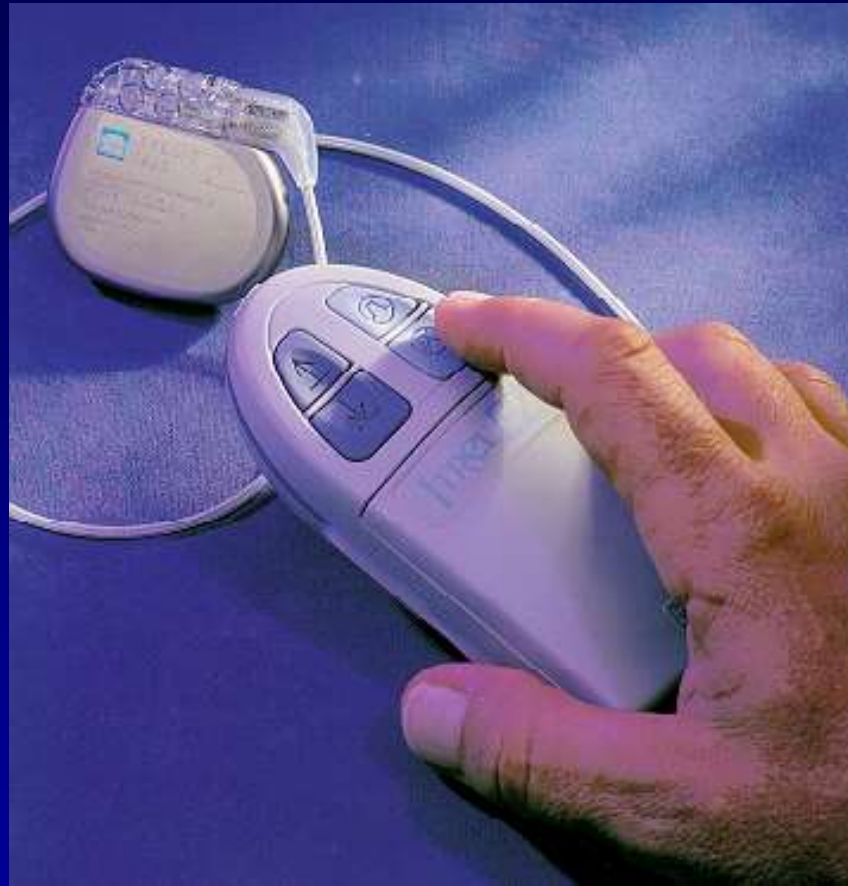
– **Percutanea**
  - » **anestesia locale**
  - » **stimolazione intraoperatoria**

– **Laminectomia**
  - » **anestesia generale**

– **Stimolazione di prova (1- 4 settimane)**
  - » riduzione del dolore **>50% = stimolazione cronica**

– **Impianto del generatore di corrente**

# La stimolazione del midollo spinale

## TECNICA

- **Percutanea**
  - » **anestesia locale**
  - » **stimolazione intraoperatoria**
- **Laminectomia**
  - » **anestesia generale**
- **Stimolazione di prova (1- 4 settimane)**
  - » riduzione del dolore **>50-40% = stimolazione cronica**
- **Impianto del generatore di corrente**

# La Neuromodulazione nel trattamento del dolore

## Stimolazione del midollo spinale - Indicazioni

1. Failed back surgery syndrome
2. Vasculopatia ostruttiva periferica
3. Angina
4. Nevralgia post-herpetica
5. Dolore del paraplegico
6. Dolore da neuropatia periferica
7. CRPS
8. Arto fantasma

# La stimolazione del midollo spinale

## FATTORI PROGNOSTICI

- parestesie che coprano la zona del dolore
- periodo di stimolazione di prova
- distribuzione del dolore
- durata del dolore
- intensità del dolore
- sesso
- capacità funzionali
- attività lavorativa, risarcimenti
- MMPI, McGill painquestionnaire

# Stimolazione del midollo spinale: simpaticolisi funzionale

Fig. 2. HR during physiological sympathetic activations before (white circles) and during SCS (black circles).

Fig. 3. HR during physiological parasympathetic activation before (white circles) and during SCS (black circles). RT CSP = right carotid sinus pressure; LT CSP = left carotid sinus pressure.

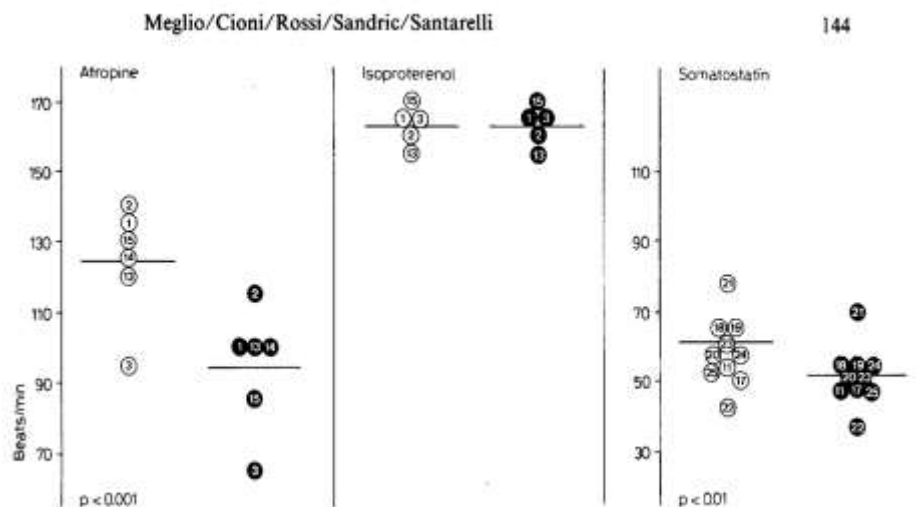



Fig. 4. HR after drug injection before (white circles) and during SCS (black circles).

# Stimolazione del midollo spinale: meccanismi biochimici

**Sono state studiate le concentrazioni liquora-li di somatostatina, CSK, VIP, neurotensine, sostanza P (?)**

**Studi nel ratto ipotizzano che la SCS possa agire aumentando l'attività di interneuroni inibitori gabaergici.**

# LA SCS NELLA FAILED BACK SURGERY SYNDROME

## FBSS

Sindrome dolorosa cronica alla schiena e/o agli arti inferiori persistente dopo uno o più interventi chirurgici al rachide lombo-sacrale.

15-20% dei pazienti operati.

Dolore misto: neuropatico e nocicettivo

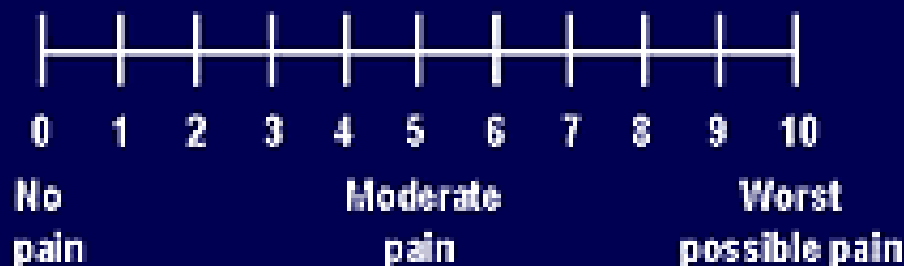
**Cause di persistenza del dolore:**

- diagnosi inappropriata
- chirurgia inappropriata
- recidiva  ernia discale
- instabilità
- cicatrice
- discite

# LA SCS NELLA FAILED BACK SURGERY SYNDROME

## RISULTATI A 5 ANNI

| *Autore* | *# pz* | *eccell/buoni* |
|---|---|---|
| • North R et a | 102 | 70% |
| • Fiume D et al | 55 | 56% |
| • Rainov N et al | 32 | 66% |
| • Devulder J et al | 66 | 65% |
| • Meglio et al | 193 | 60% |

# Pain Assessment Scales

1. Portenoy RK, Kanner RM, eds. *Pain Management: Theory and Practice.* 1996:8-10.
2. Wong DL. *Waley and Wong's Essentials of Pediatric Nursing 5th ed.* 1997:1215-1216.
3. McCaffery M, Pasero C. *Pain: Clinical Manual.* Mosby, Inc. 1999:16.

# LA SCS NELLA FAILED BACK SURGERY SYNDROME

## STUDI RANDOMIZZATI

### Reintervento vs SCS

(North R et al, 1995)

- 67% dei pazienti ri-operati hanno richiesto la SCS
- 17% dei pazienti stimo-lati hanno richiesto il reintervento

### Infusione spinale di oppiacei vs SCS

(Hassenbush et al, 1995)

- 13% di successi dopo infusione spinale di oppiacei
- 62% di successi dopo SCS

# LA SCS NELLA FAILED BACK SURGERY SYNDROME

## STUDIO PROCESS

214 patients assessed for eligibility

51 patients excluded for predominant back pain
28 excluded for other reasons
35 refused randomisation

100 patients randomised

48 assigned to CMM group

52 assigned to SCS group

4 withdrew consent

2 withdrew consent

44 in 6-months analysis*

50 in 6-months analysis

By 12-months follow-up:

16 received CMM only (includes 4 patients who requested to cross to SCS but failed trial screening)
28 crossed to SCS

By 12-months follow-up:

45 received SCS only
5 crossed to CMM

1 lost to follow-up
2 withdrew consent

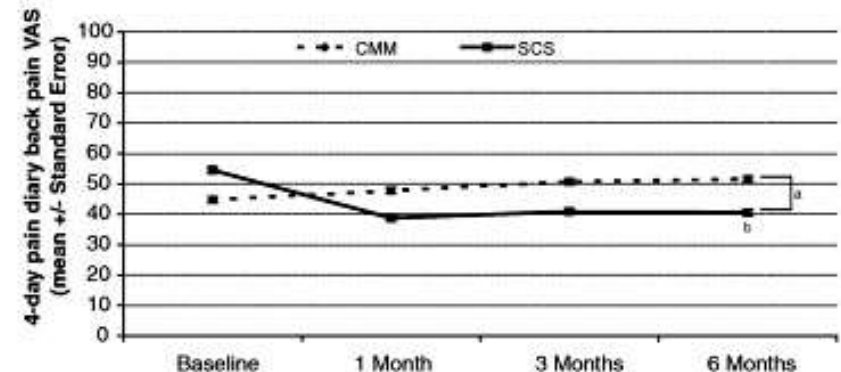
2 lost to follow-up
1 withdrew consent

41 in 12-months analysis

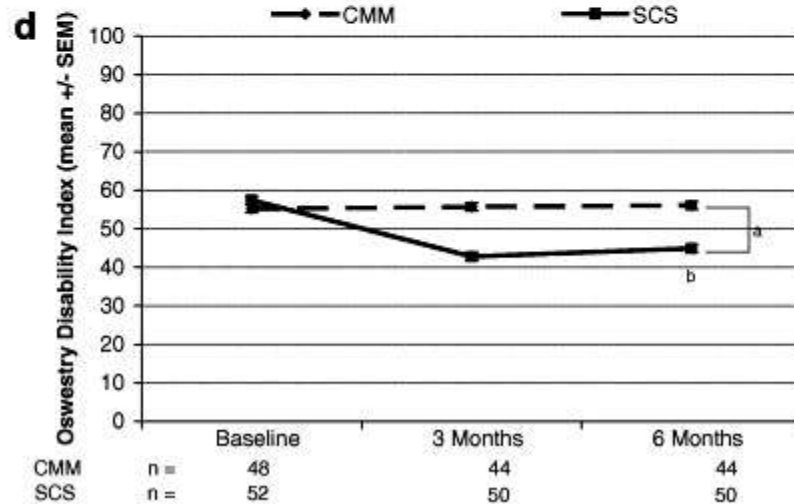
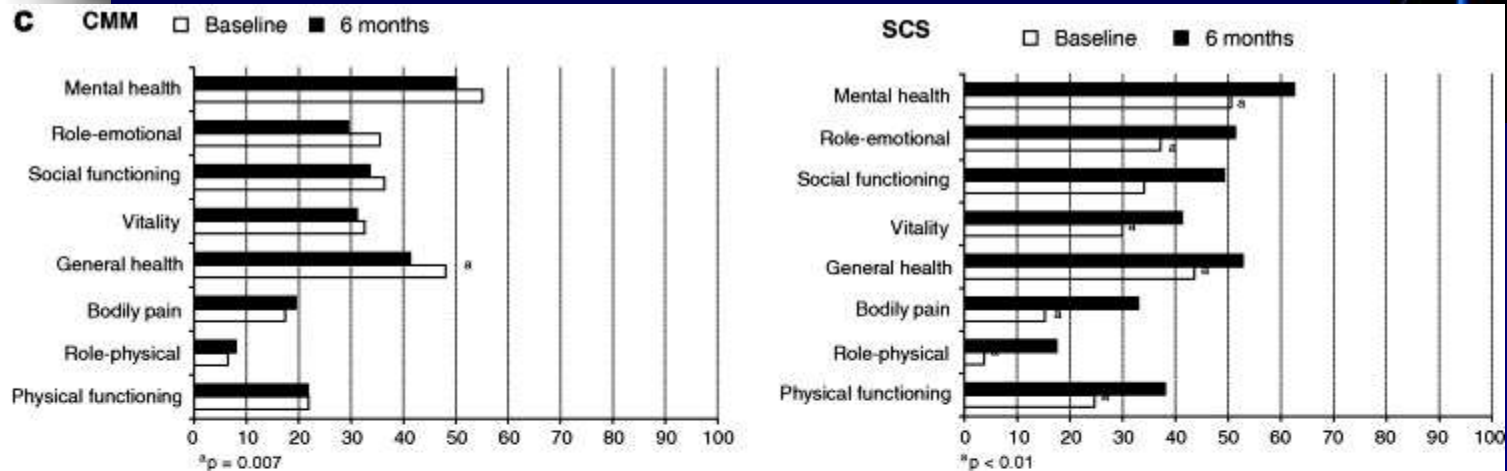
47 in 12-months analysis

LA SCS NELLA FAILED BACK SURGERY SYNDROME
STUDIO PROCESS

a
CMM
SCS
Percent of patients achieving ≥50% leg pain relief
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.02
0.47
0.09
0.56
0.09
0.48
a
1 Month
3 Months
6 Months
n =
47
51
44
50
44
50
Months
[a]p < 0.001 between groups at 6 months

b
4-day pain diary leg pain VAS (mean +/- Standard Error)
CMM
SCS
100
90
80
70
60
50
40
30
20
10
0
Baseline
1 Month
3 Months
6 Months
c
a
b
[a]p < 0.001 between groups at 6 months
[b]p < 0.001 in SCS group between 6 months and baseline
[c]p = 0.03 in CMM group between 6 months and baseline

4-day pain diary back pain VAS (mean +/- Standard Error)
CMM
SCS
100
90
80
70
60
50
40
30
20
10
0
Baseline
1 Month
3 Months
6 Months
a
b
[a]p = 0.008 between groups at 6 months
[b]p = 0.007 in SCS group between 6 months and baseline

# LA SCS NELLA FAILED BACK SURGERY SYNDROME

## STUDIO PROCESS

# LA SCS NELLA ANGINA PECTORIS REFRATTARIA

**Di Pede et al, Am J Cardiol 91:951-955, 2003**

104 pazienti, follow-up medio: 13.2 mesi

| | pre-SCS | max FU |
|---|---|---|
| Episodi anginosi totali/sett | 10.2 | 3.2 |
| Episodi anginosi a riposo/sett | 6 | 2 |
| Episodi anginosi da sforzo/sett | 4 | 1.2 |
| Pasticche di Nitroglicerina/sett | 8.9 | 2 |
| CCS angina class | 3.4 | 2.2 |
| Ricoveri in ospedale/6mesi | 2 | 0.6 |
| Giorni in ospedale/6mesi | 20 | 2.2 |

**NB modificazioni tutte statisticamente altamente significative**

# LA SCS NELLA ANGINA PECTORIS REFRATTARIA

**McNab et al, Eur Heart J 27: 1048-1053, 2006**

**SCS (34 pz) vs Percutaneous Myocardial Revascularization (34 pz)**

| | Exercise treadmill time (min) | |
|---|---|---|
| | baseline | 12 months |
| **SCS** | **6.4+/-3.5** | **7.1+/-0.1** |
| **PMR** | **7.4+/-3.7** | **7.1+/-0.7** |

**No difference in effectiveness between SCS and PMR**

**“Compared to CABG, SCS provided similar benefits in terms of pain control and quality of life improvement in patients with an increased risk of surgical complications….but SCS is significan-tly less expensive” Buchser et al, 2006**

# LA SCS NELLA SINDROME X

**Lanza et al, Eur Heart J 26: 983-989, 2005**

10 pazienti, 3sett: SCS-on vs 3 sett: SCS-off

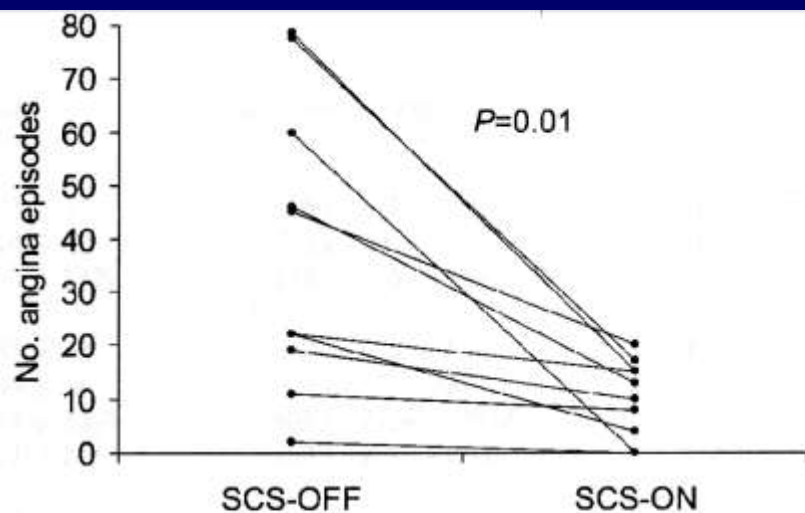



**Figure 2** Number of angina episodes according to structured patients' diaries, during the 2-week periods with (SCS-ON) or without (SCS-OFF) spinal cord stimulation.

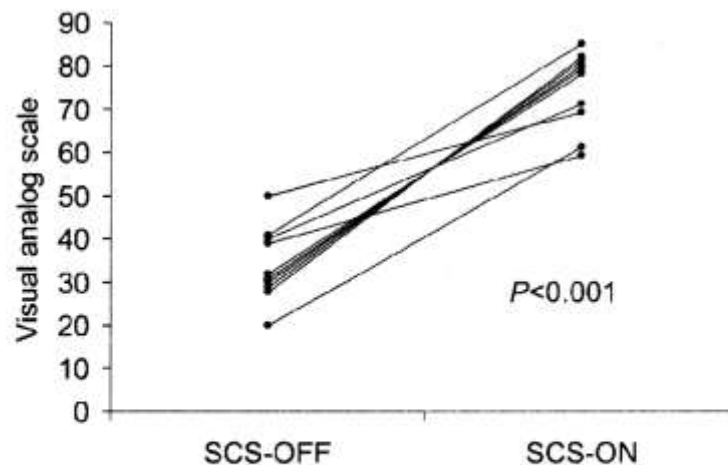



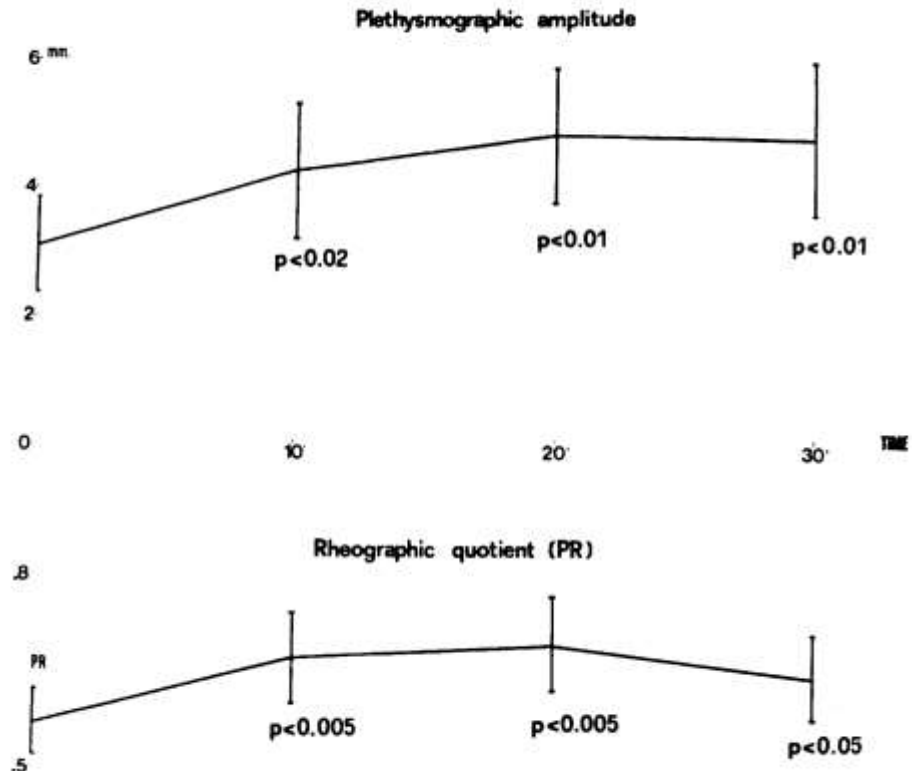
**Figure 3** Rating of quality of life by patients, according to the EuroQOL visual analogue scale, during the periods with (SCS-ON) or without (SCS-OFF) spinal cord stimulation.

# LA SCS NELLA VASCULOPATIA OSTRUTTIVA PERIFERICA

**Meglio et al, 1981, 1988**

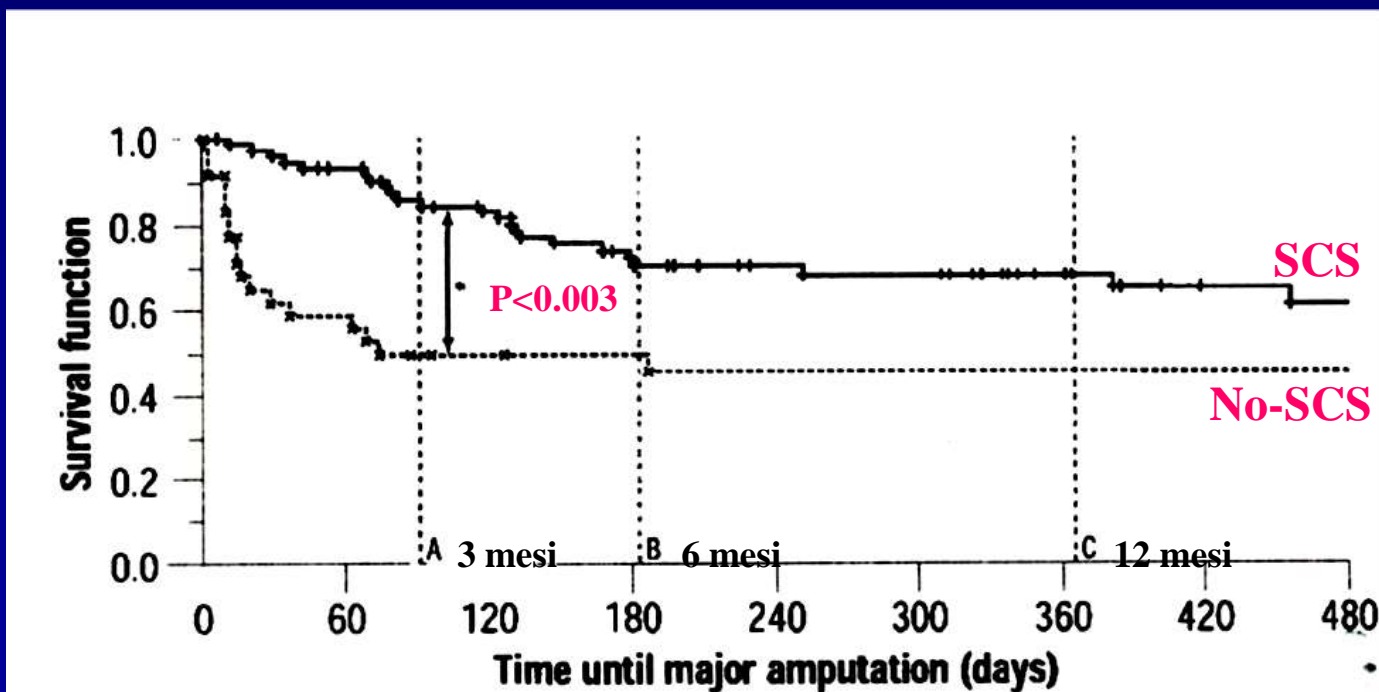
**43 pazienti: 15 stadio IIIA, 22 stadio IIIB, 6 stadio IV di Leriche-Fontaine**

**Fu medio: 20.78mesi**

**79% dei pazienti mantengono 83% di analgesia al max FU**

# LA SCS NELLA ISCHEMIA CRITICA DEGLI ARTI

**Amann et al, Eur J Vasc Endovasc Surg 26:280-286,2003**

**Results of the European Peripheral Vascular Disease Outcome Study: 112 pazienti, follow up 12 - 18 mesi**

**valutano “limb survival”**

Survival function
1.0
0.8
0.6
0.4
0.2
0.0
SCS
No-SCS
$P<0.003$
A 3 mesi
B 6 mesi
C 12 mesi
0 60 120 180 240 300 360 420 480
Time until major amputation (days)

# LA SCS NELLA ISCHEMIA CRITICA DEGLI ARTI

Amann et al, Eur J Vasc Endovasc Surg 26:280-286,2003

**Results of the European Peripheral Vascular Disease Outcome Study:**

**112 pazienti, valutano “limb survival” :**

**39 pz: no-SCS; 41 pz: SCS-Match*; 32 pz: SCS-no-Match**

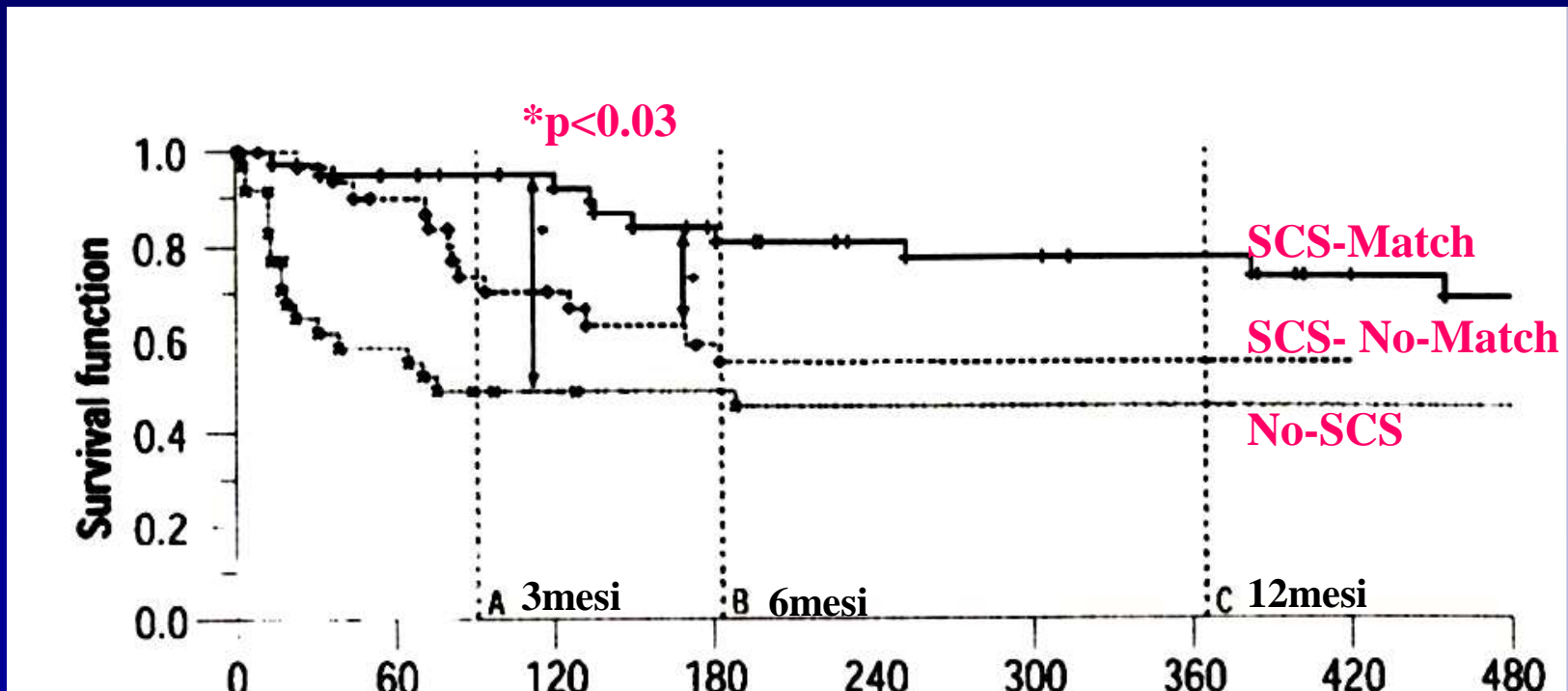
*p<0.03

Survival function

1.0
0.8
0.6
0.4
0.2
0.0

0 60 120 180 240 300 360 420 480

A 3mesi
B 6mesi
C 12mesi

SCS-Match
SCS- No-Match
No-SCS

***SCS-Match:TcpO2<30mmHg + parestesie corrette + effetto antalgico dopo test di 72h**

# LA SCS NELLA ISCHEMIA CRITICA DEGLI ARTI

Amann et al, Eur J Vasc Endovasc Surg 26:280-286,2003

**Results of the European Peripheral Vascular Disease Outcome Study:**

**112 pazienti, valutano "limb survival" :**

**39 pz: no-SCS; 41 pz: SCS-Match*; 32 pz: SCS-no-Match**

## CONCLUSIONI

**La SCS presenta una percentuale di limb saving significativamente più alta paragonata al trattamento medico, soprattutto se la TcpO2 è compresa tra 10 e 30 mmHg e se vi è risposta antalgica al test di prova (78% di limb saving)**

# LA SCS NELLA ISCHEMIA CRITICA DEGLI ARTI

**Ubbink et al, J Pain Symptom Manage 31:S30-S35, 2006**

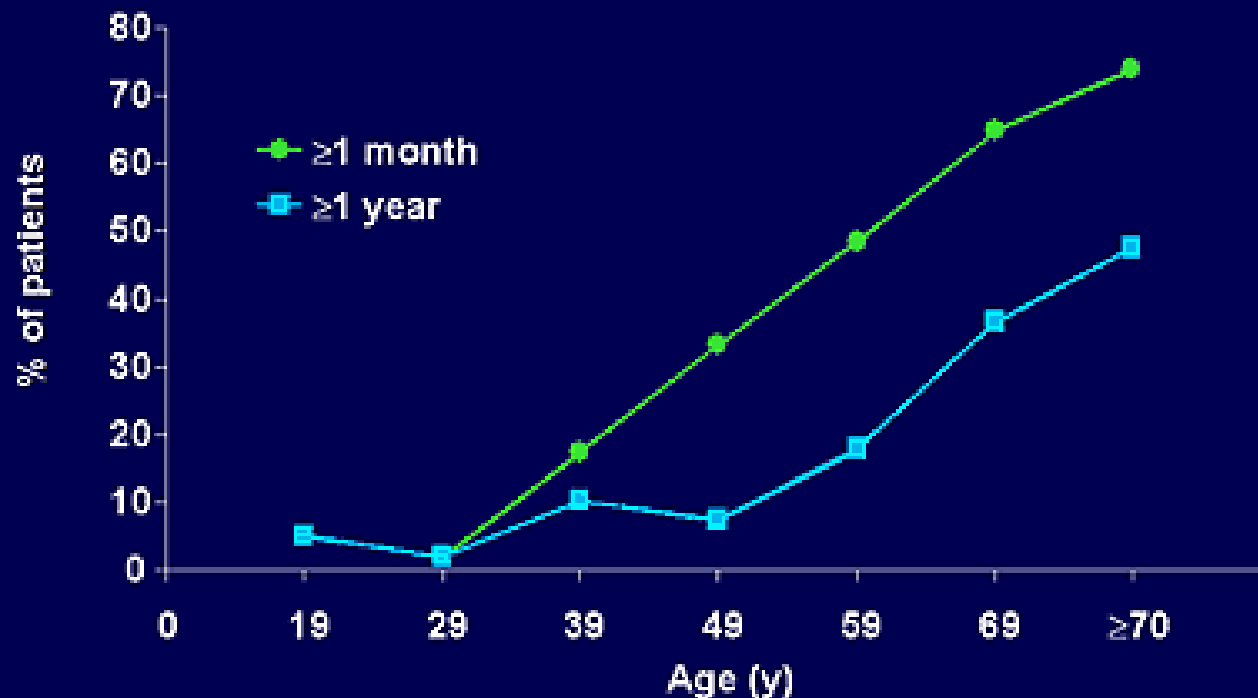
## Metanalisi di 444 pazienti

**Confermano un limb saving fino all’83% a 12 mesi se i pz vengono selezionati in base alla TcpO2.**

**La SCS è più efficace del trattamento medico nella ischemia critica dell’arto, quando oltre a trattare il dolore si voglia salvare il paziente dall’amputazione**

**Se lo scopo della SCS è solo il trattamento del dolore, i costi della SCS ne limitano l’uso, essendoci delle valide alternative meno costose.**

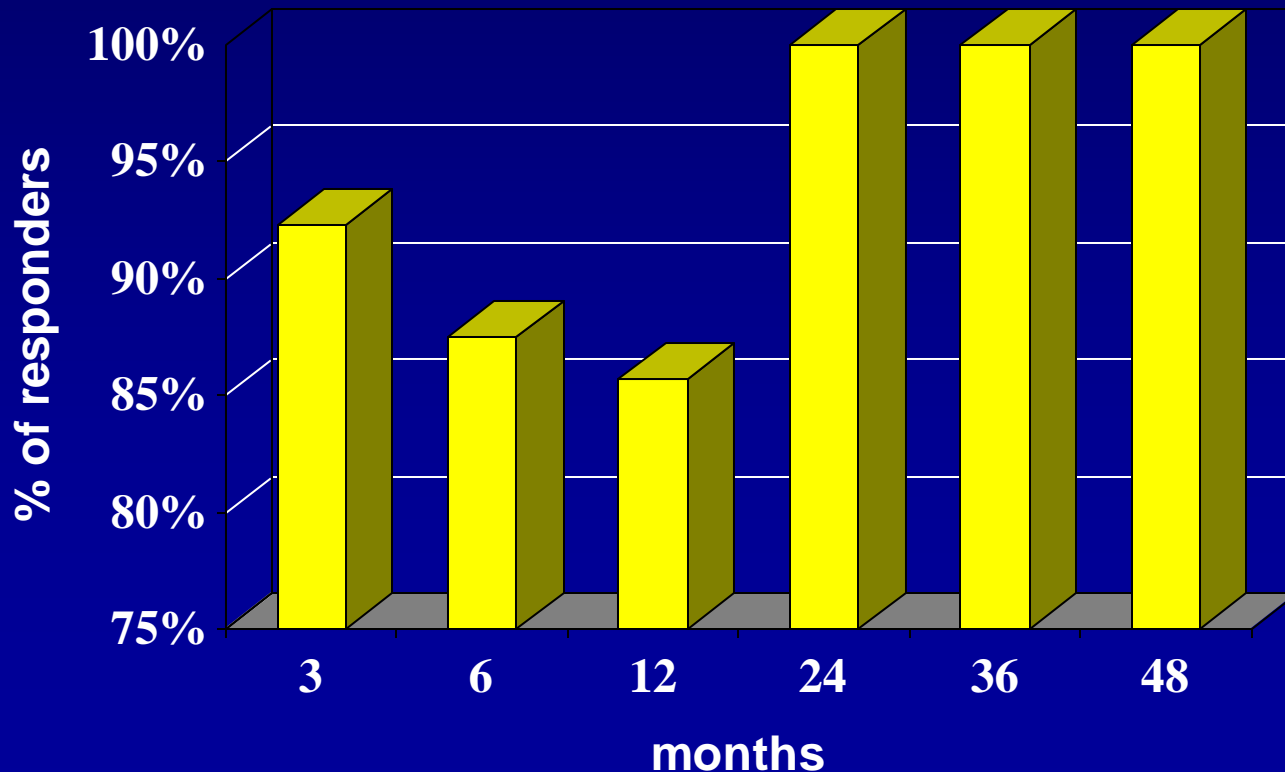
# LA SCS NELLA NEVRALGIA POST-HERPETICA

## Percentages of Herpes Zoster Patients With Persistent Pain



Adapted from DeMorgas JM, Kierland RR. *Arch Dermatol.* 1957;75:193-196.

# LA SCS NELLA NEVRALGIA POST-HERPETICA

- Risultati al test: 62% di responders
- Risultati a lungo termine:

| months | % of responders |
|---|---|
| 3 | |
| 6 | |
| 12 | |
| 24 | |
| 36 | |
| 48 | |

# LA SCS NEI DOLORI DA LESIONE SPINALE

1981-1991: 25 pazienti

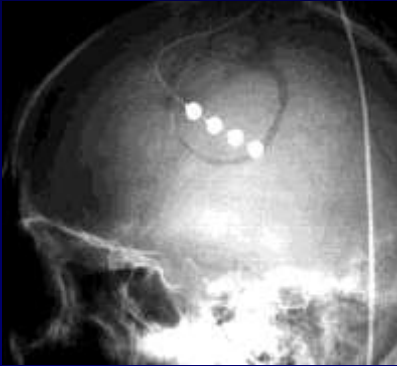
- Risultati al test: 35% di responders
- Risultati a lungo termine: 15% di responders

# LA SCS NEI DOLORI DA LESIONE SPINALE

1981-1991: 25 pazienti

**Qualità del dolore e responders**

| | |
|---|---|
| • urente | 7% |
| • spasmi dolorosi | 38% |
| • lacerante | 0% |
| • costrittivo | 50% |

# CHRONIC MOTOR CORTEX STIMULATION FOR PAIN

**Tsubokawa T. et al.**
**Acta Neurochirurgica 1991**

HIRAYAMA T., TSUBOKAWA T., KATAYAMA Y., YAMAMOTO Y., KOYAMA S.
*Chronic changes in activity of thalamic relay neurons following spinothalamic tractotomy in cat. Effects of motor cortex stimulation.*
Pain 5:273;1990
**Thalamic hyperactivity observed after transection of the spinothalamic tract in cats can be inhibited more efficiently by stimulation of the motor cortex rather than sensory cortex**

# CHRONIC MOTOR CORTEX STIMULATION FOR PAIN

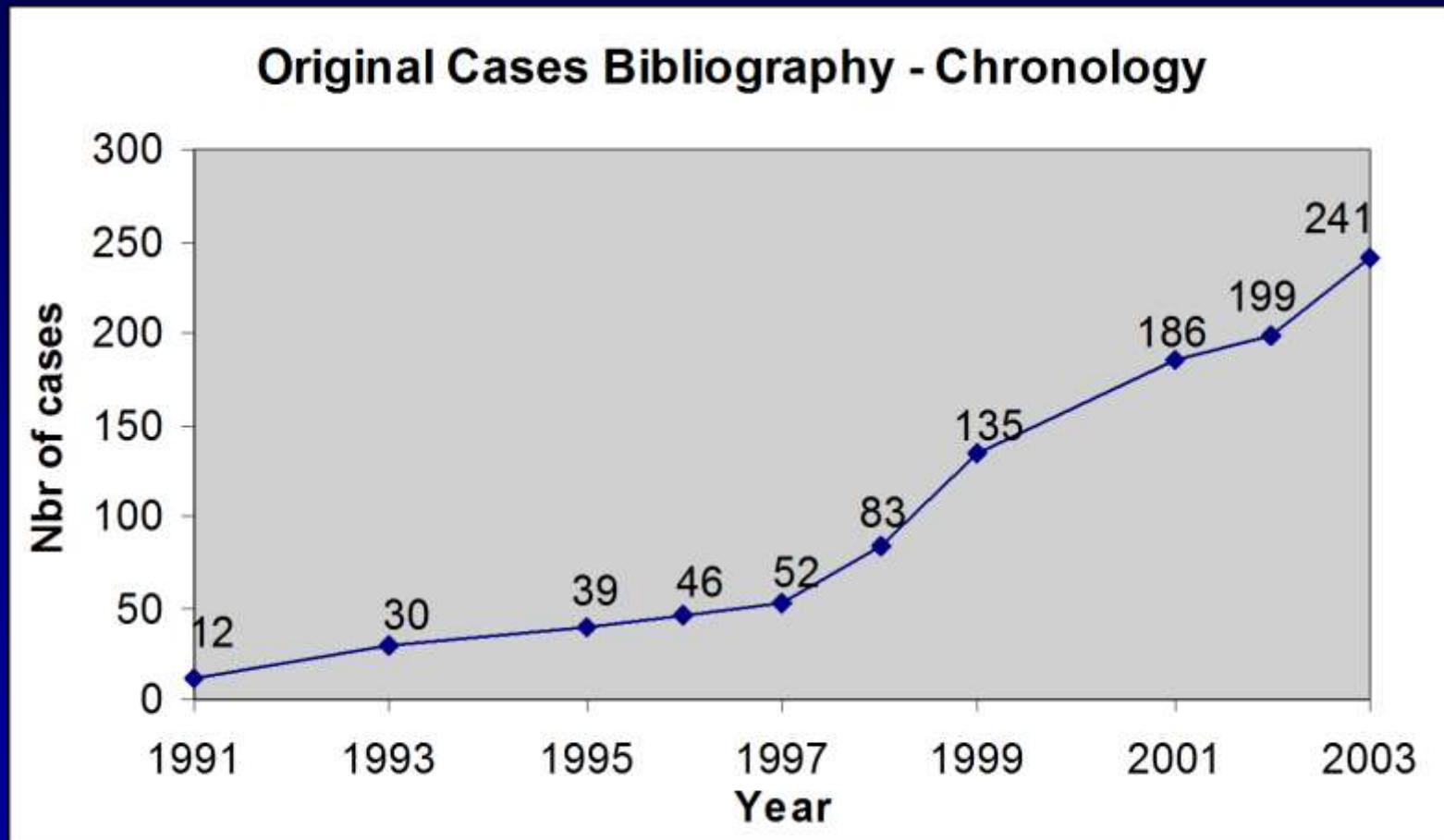
Original Cases Bibliography - Chronology

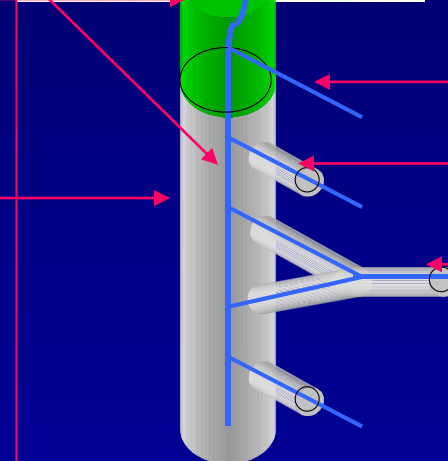
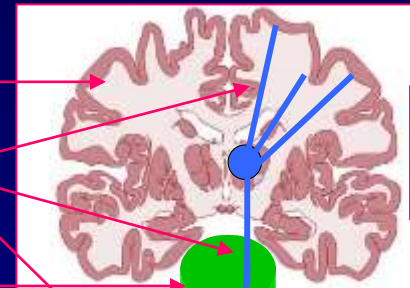
Nbr of cases

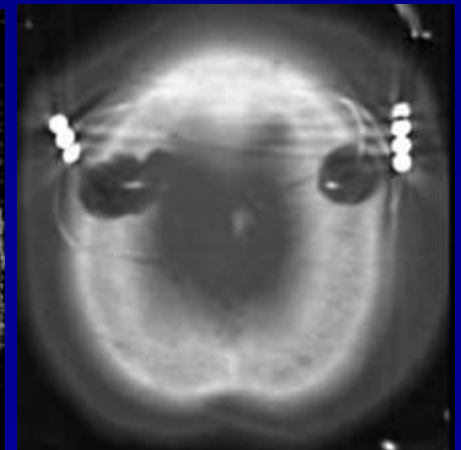
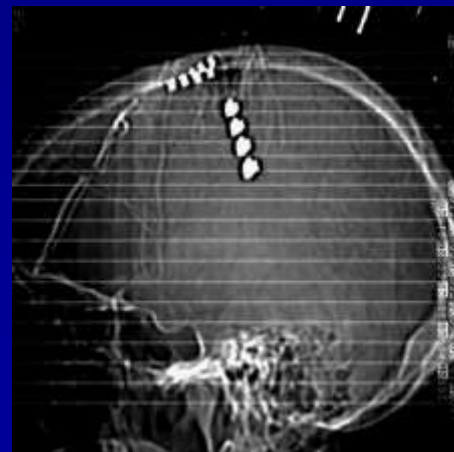
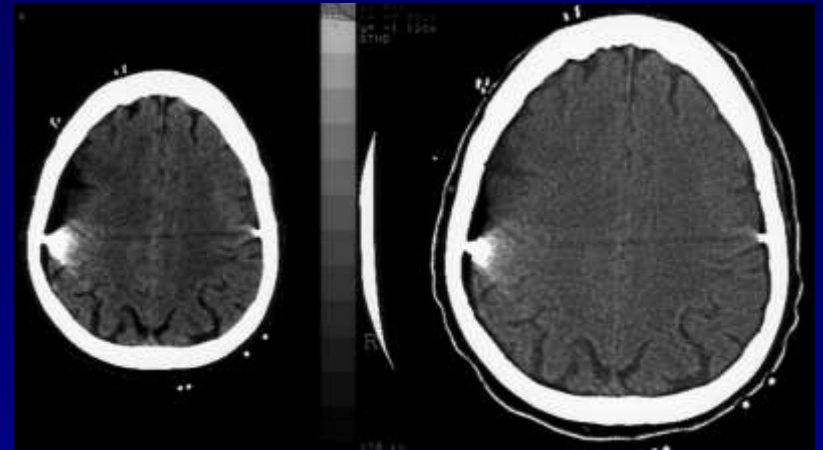
300
250
200
150
100
50
0

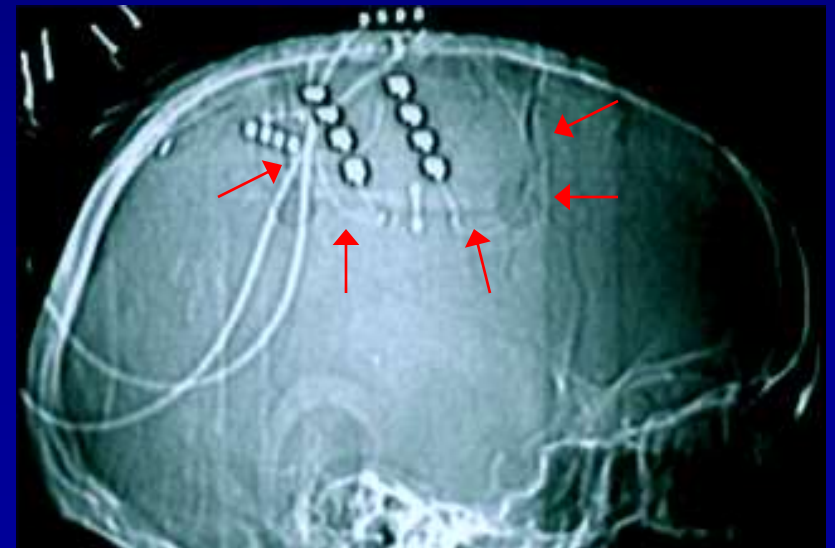
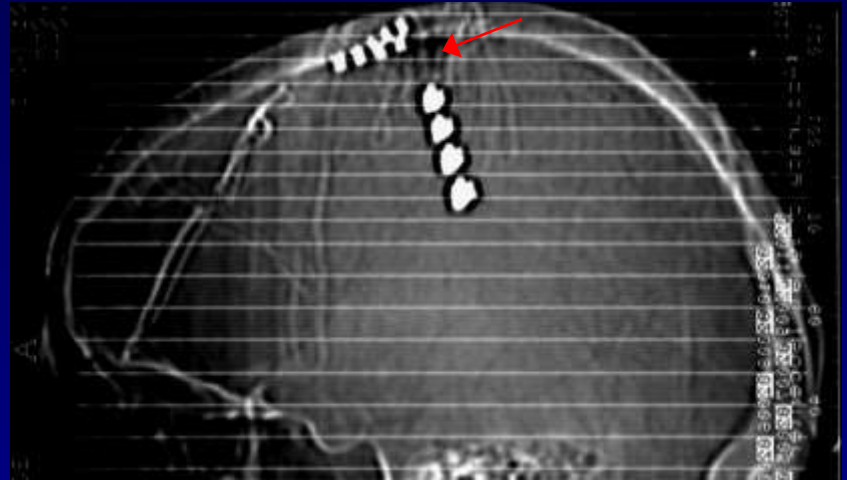
12
30
39
46
52
83
135
186
199
241

1991
1993
1995
1997
1999
2001
2003

Year

# CHRONIC MOTOR CORTEX STIMULATION FOR PAIN: INDICATIONS

| Diagnosis | No patients |
|---|---|
| Thalamic pain syndrome | 77 |
| Cortical pain | 95 |
| Basal ganglia lesions | 15 |
| Others central pain | 13 |
| Brain stem lesions | 8 |
| **Total central lesions** | **208** |
| **Spinal cord lesions** | **6** |
| **Trigeminal/facial pain** | **48** |
| Phantom limb pain | 14 |
| Peripheral nerve injury | 5 |
| Plexus avulsion pain | 10 |
| Others peripheral nerve pain | 18 |
| **Total peripheral lesions** | **47** |
| **CRPS** | **1** |
| **Various pain** | **48** |
| **Total** | **358** |

# MOTOR CORTEX STIMULATION
# INDICATIONS

- Central and peripheral deafferentation pain
- Parkinson's disease
- Stroke

# MOTOR CORTEX STIMULATION
# TECHNIQUE

- Local vs general anesthesia
- Burr hole vs craniotomy
- Extradural placement of 1 or more electrode paddles
- Chronic stimulation sub-threshold for movements and sensations
- MCS parameters: 60-210 microsec, 30-120HZ, 1-6V

# MOTOR CORTEX STIMULATION
# ELECTRODE POSITION

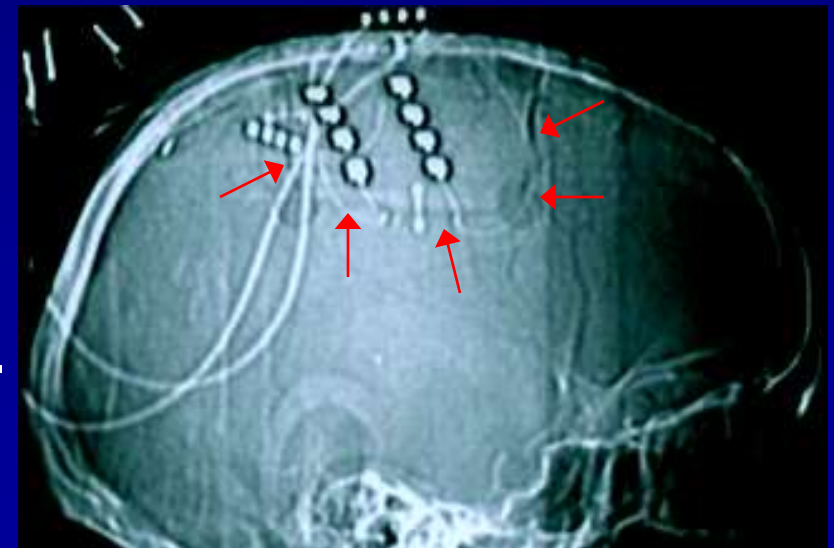
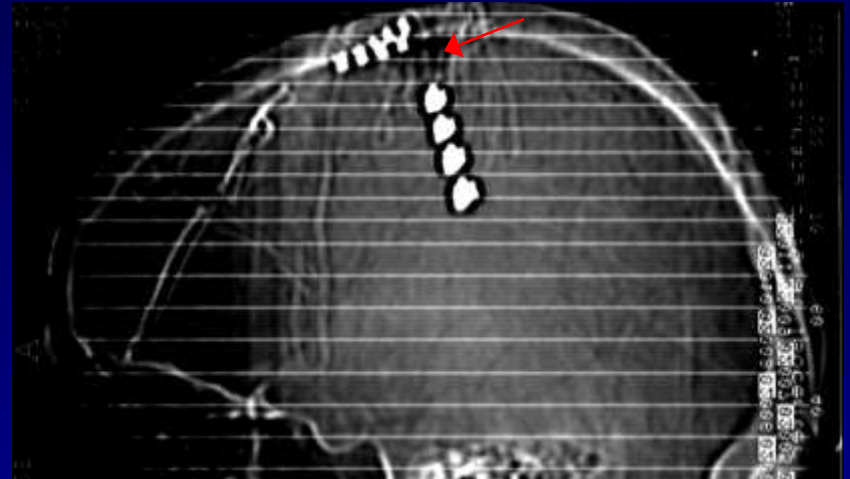
• **PAIN**

**over sensory-motor cortex, somatotopically corresponding to the painful area, perpendicular to central sulcus**

• **PARKINSON DISEASE**

**mono vs bilateral MCS, over the motor hand knob (?)**

• **STROKE**

**over the motor hand region identified by fMRI**

# Neurophysiological aspects of **motor cortex stimulation**

## Cortical Mapping Challenges

Anatomical Models

3D MRI, CT

PET, SPECT, fMRI, MRS

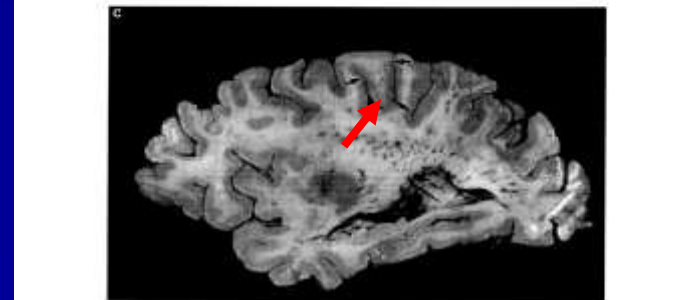
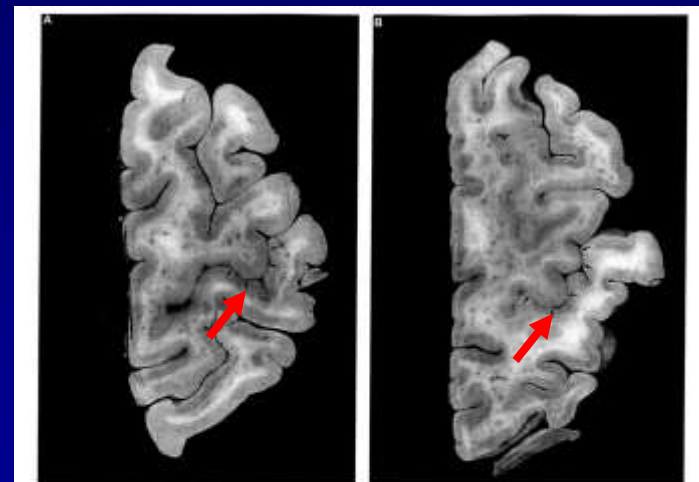
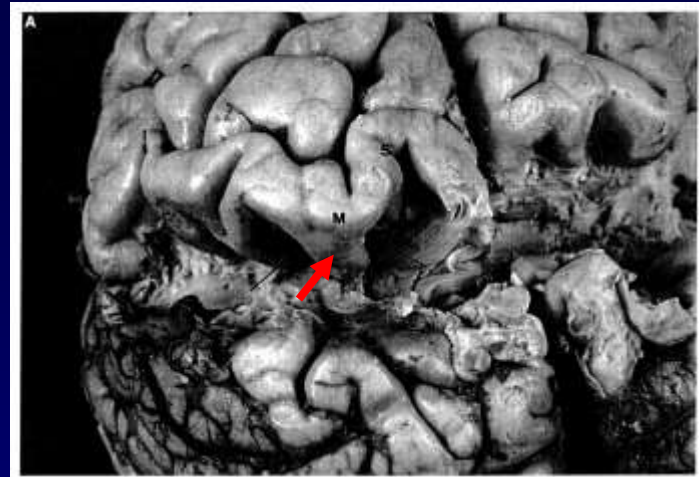
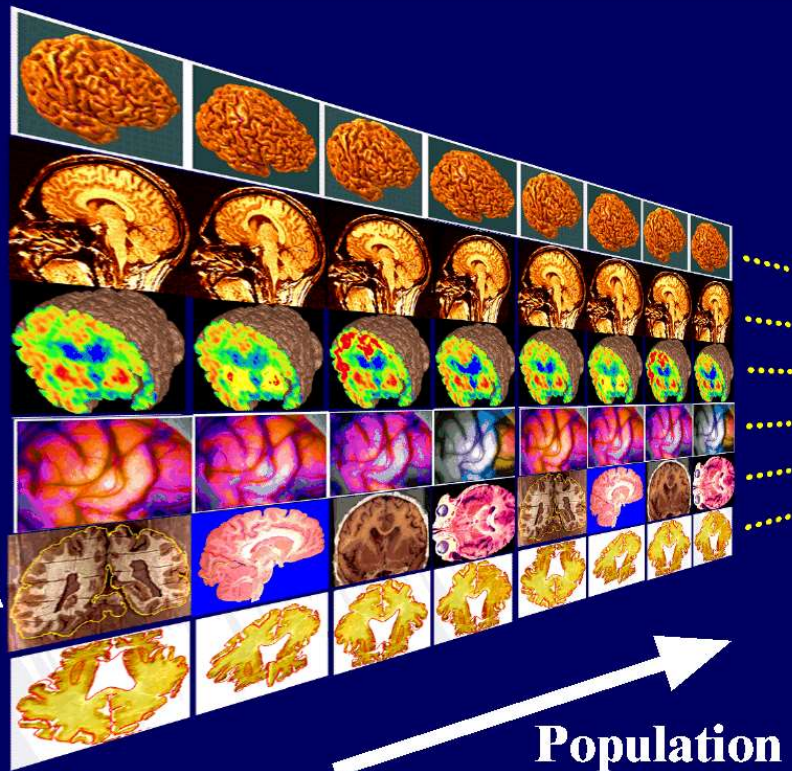
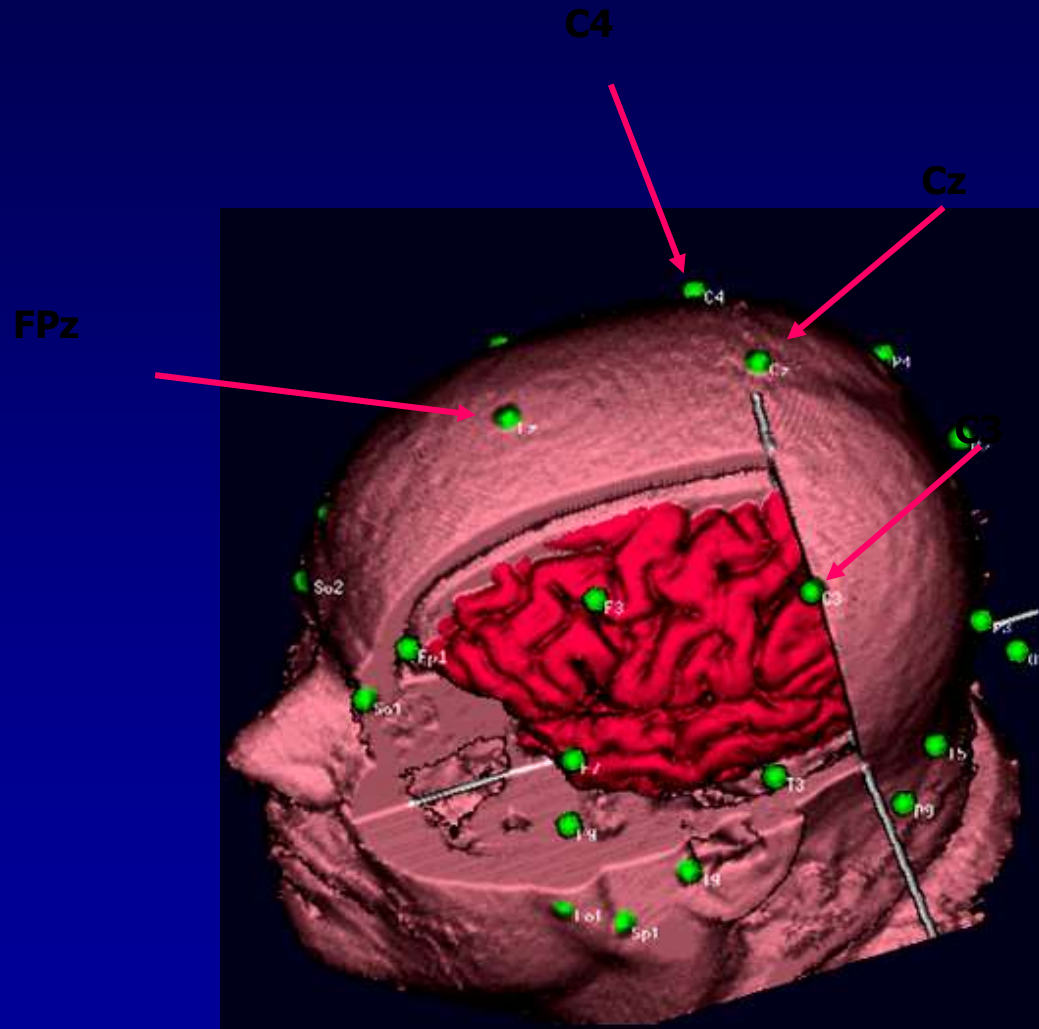
OIS, EEG, MEG

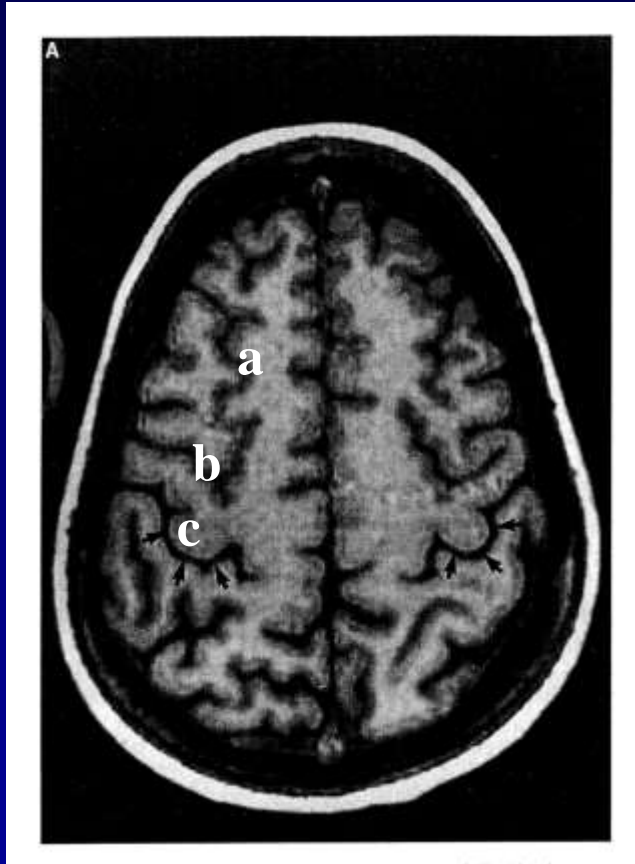
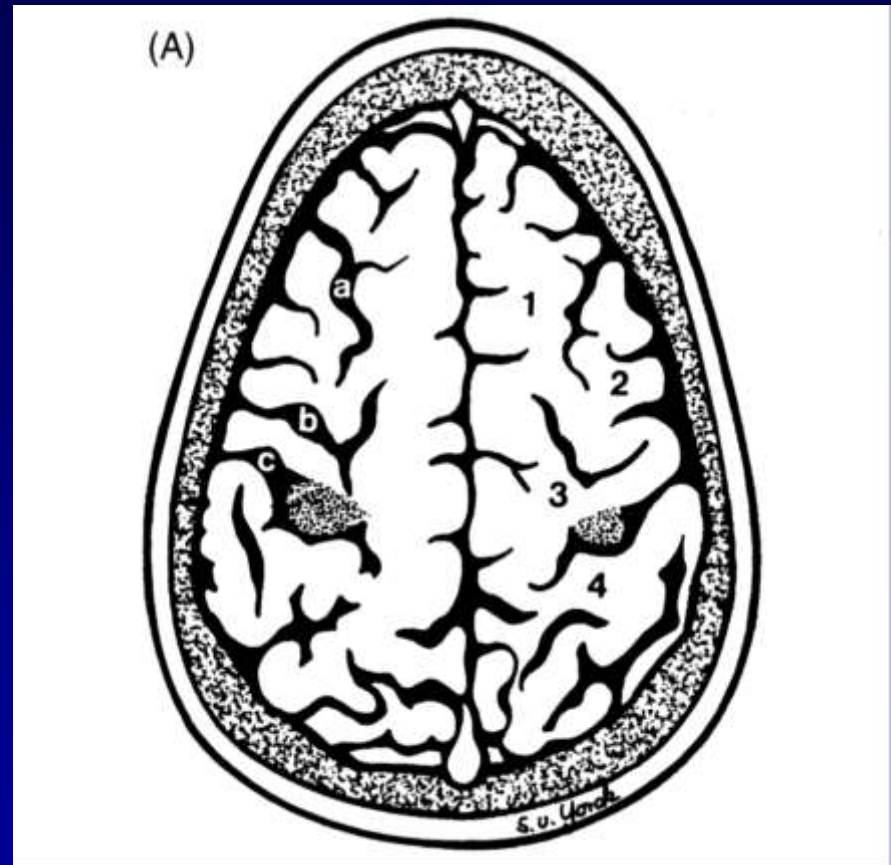
Cryo (Archit)

Histo

:

Integration

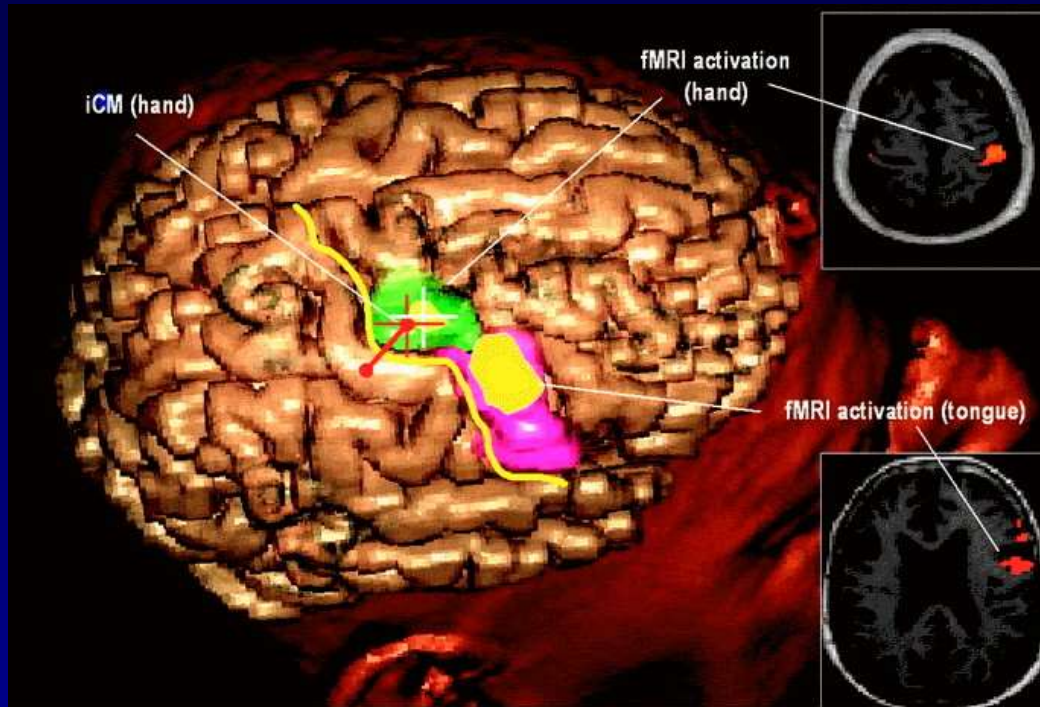
Population Variability

# Neurophysiological aspects of motor cortex stimulation

Craniometer landmarks

# Neurophysiological aspects of motor cortex stimulation

a: superior frontal sulcus
b: precentral sulcus
c: central sulcus

1: superior frontal gyrus
2: middle frontal gyrus
3: precentral gyrus
4: postcentral gyrus

# Neurophysiological aspects of motor cortex stimulation

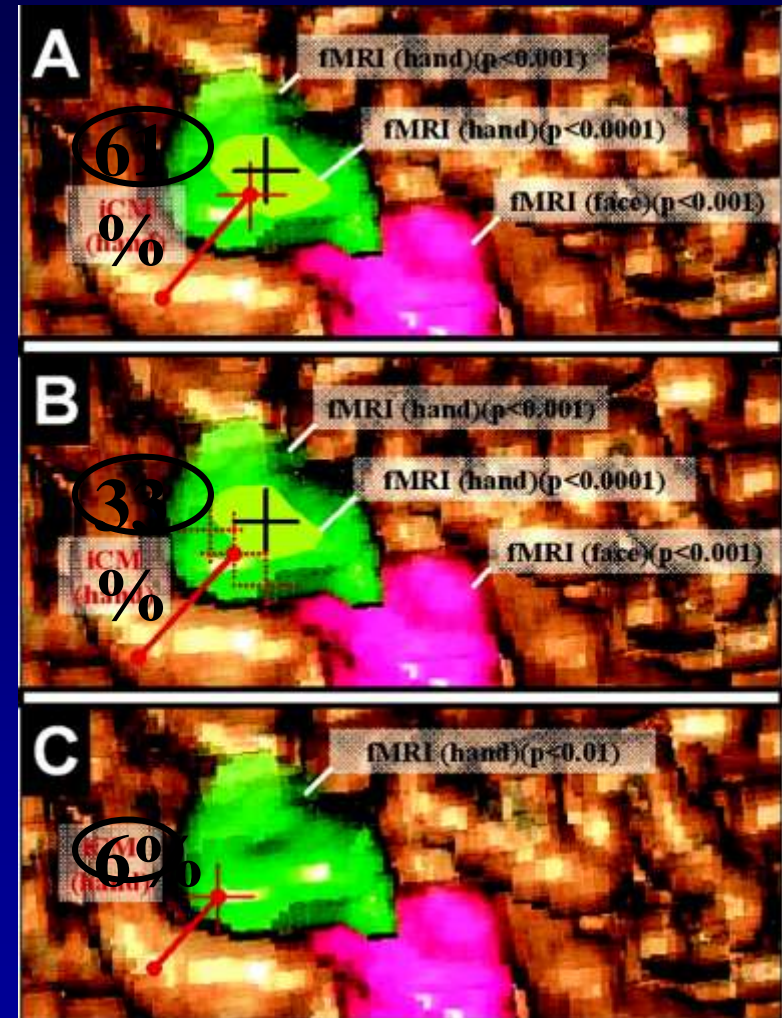
**Data from magnetoencephalography are integrated into a frameless stereotactic database by using a three-dimensional coregistration algorithm**

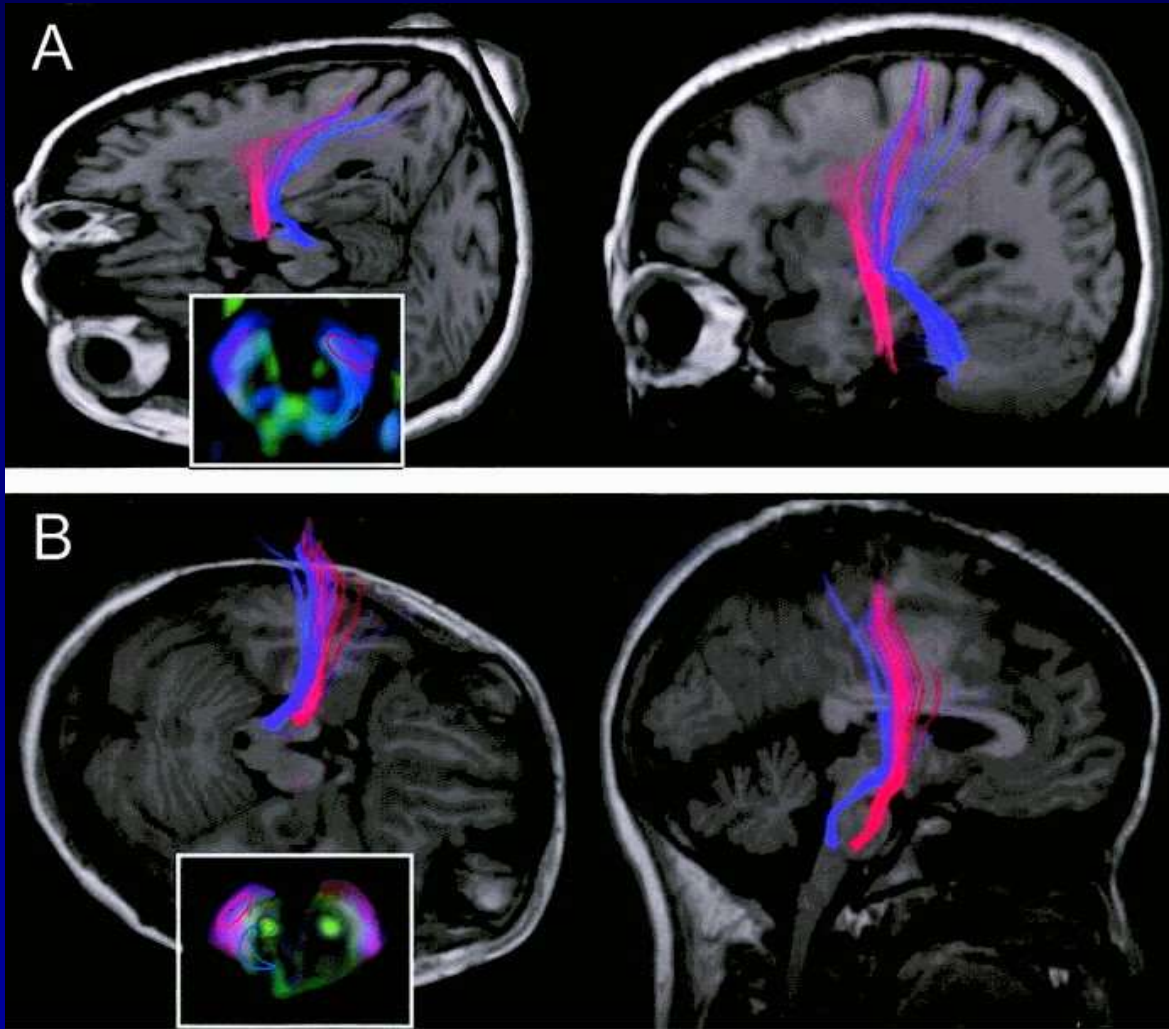
Mogilner AY, Neurosurg Focus, 2001

# Neurophysiological aspects of
# motor cortex stimulation

fMRI coregistered on 3-D T1 weighted MRI anatomical scans, matched with IOM (TIVA, SEPs + 60Hz stimulation)

61% (A): correspondence between fMRI and IOM (mean di-stance 3.8mm+/-1.3mm)

33% (B): ambiguous IOM (artifacts, anesthesia, SEPs attenua-tion, diffuse motor response, sensorimotor disconnection)

6% (C): poor fMRI and IOM localization

Pirotte et al, Neurosurg Suppl, 2005

# Neurophysiological aspects of motor cortex stimulation

**DTI**

**It is a mathematical probability function, not an anatomical image.**

Kamada et al,
Neurosurgery Suppl, 2005

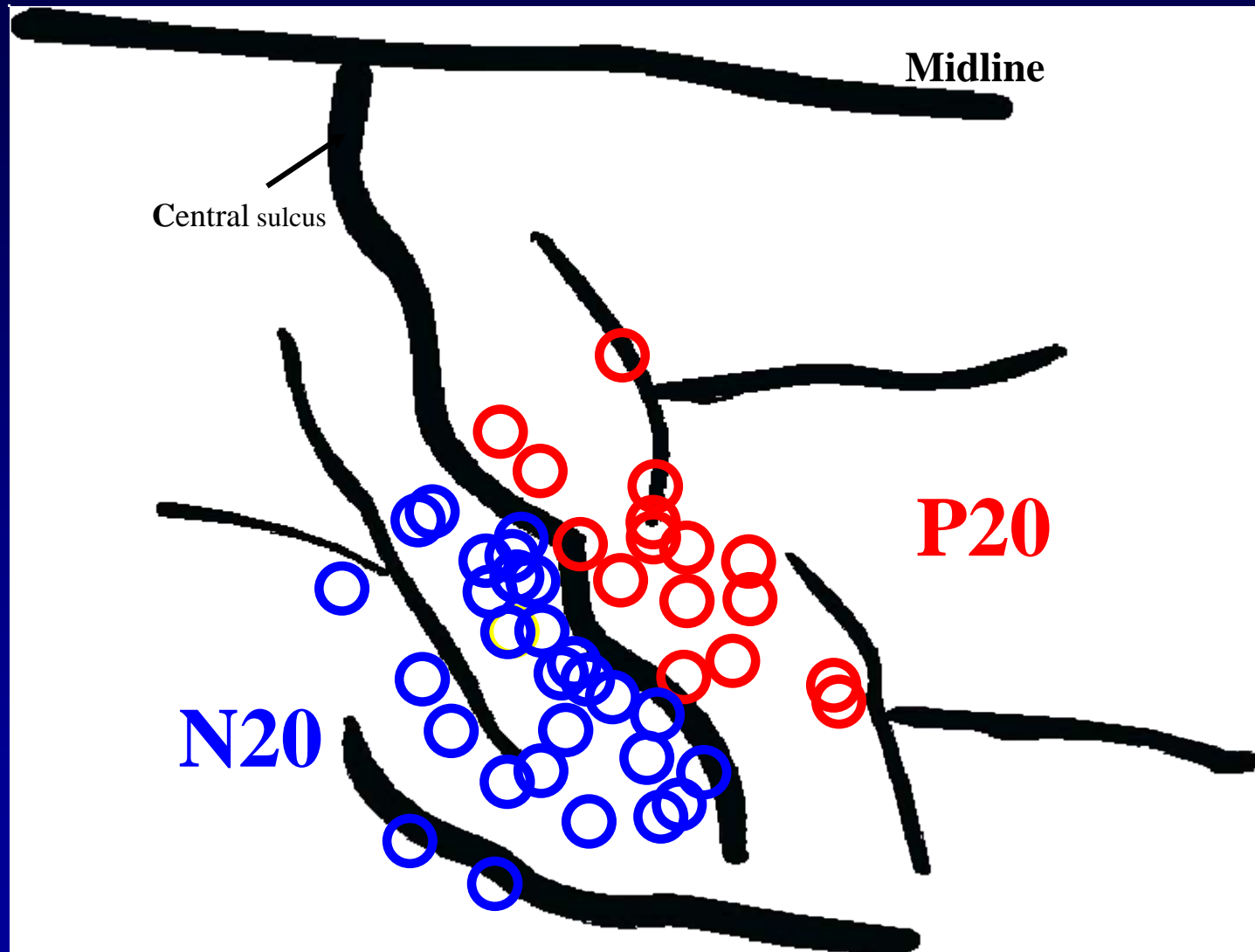
# Neurophysiological aspects of **motor cortex stimulation**

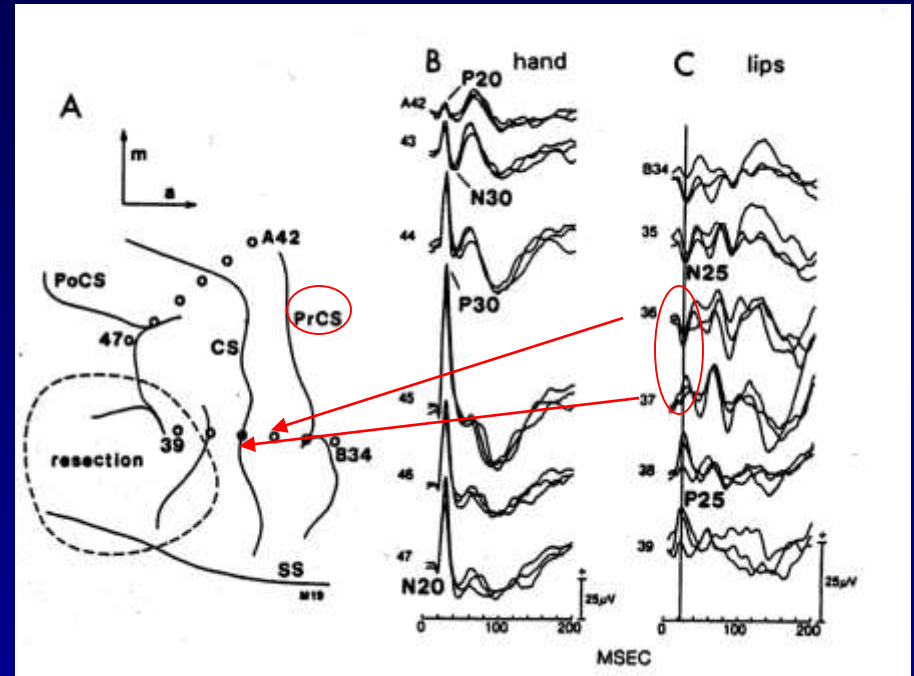
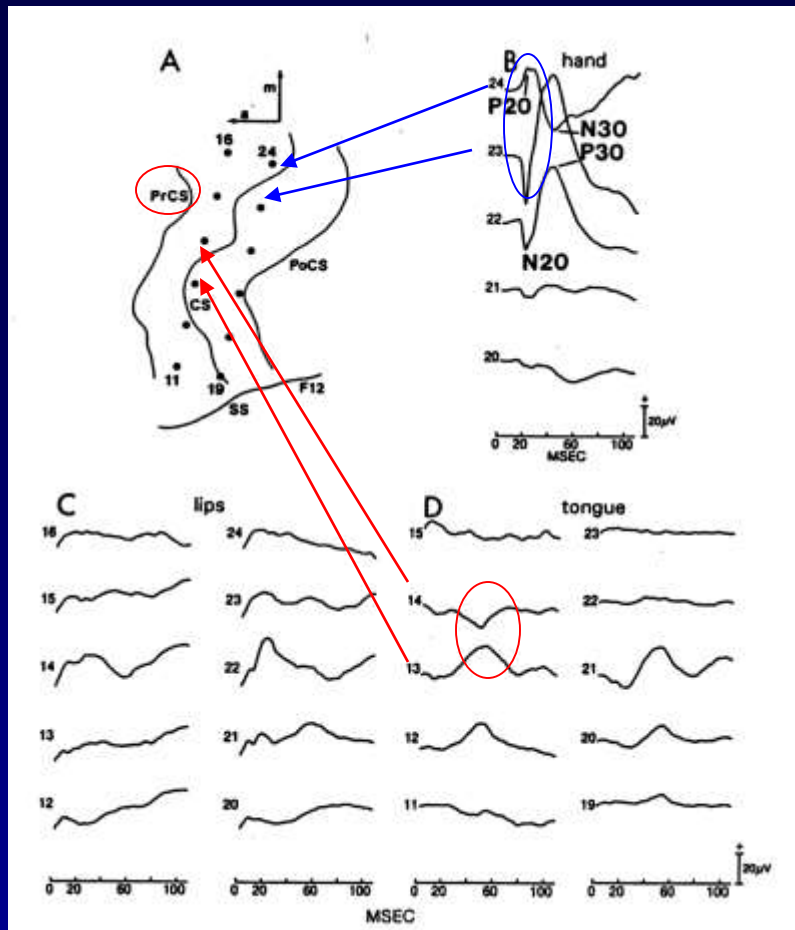
## SEPs

**Electrical stimulation of the right median nerve at the wrist (0.5ms, 23.3 mA, 4.7 Hz).**

**Recordings from extradural electrode (0-FPz, 1-FPz, 2-FPz, 3-FPz).**

3 2 1 0

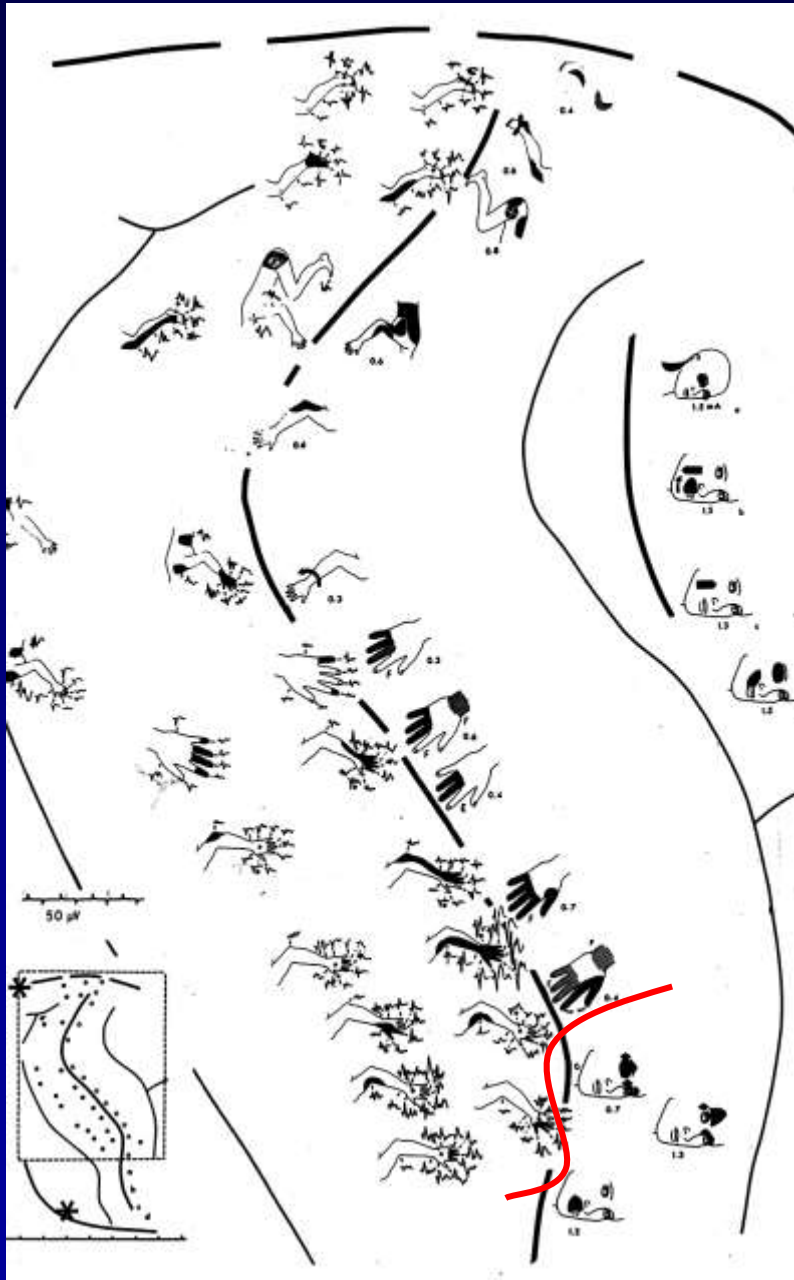
# Neurophysiological aspects of motor cortex stimulation

From: Nguyen JP et al, Pain, 1999

# Neurophysiological aspects of **motor cortex stimulation**

**TRIGEMINAL SEPs** (McCarthy et al, 1993)

"Polarity inversion of potentials across the sulcus is a less reliable criterion for trigeminal SEPs than for median nerve SEPs"

**TIBIAL NERVE SEPs ?**

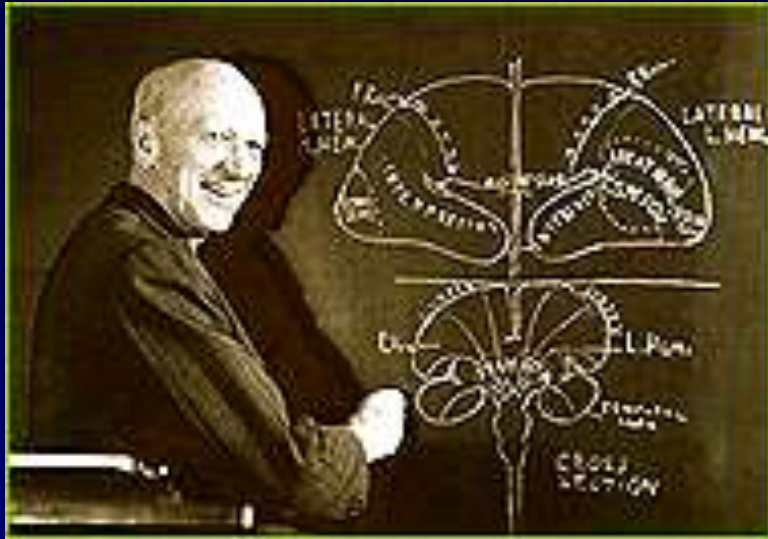
# Neurophysiological aspects of

# motor cortex stimulation

**POST vs PRE CENTRAL REPRESENTATION**

**The face - arm boundary is situated more laterally on the post-central gyrus than on the precentral**

Woolsey et al, 1979

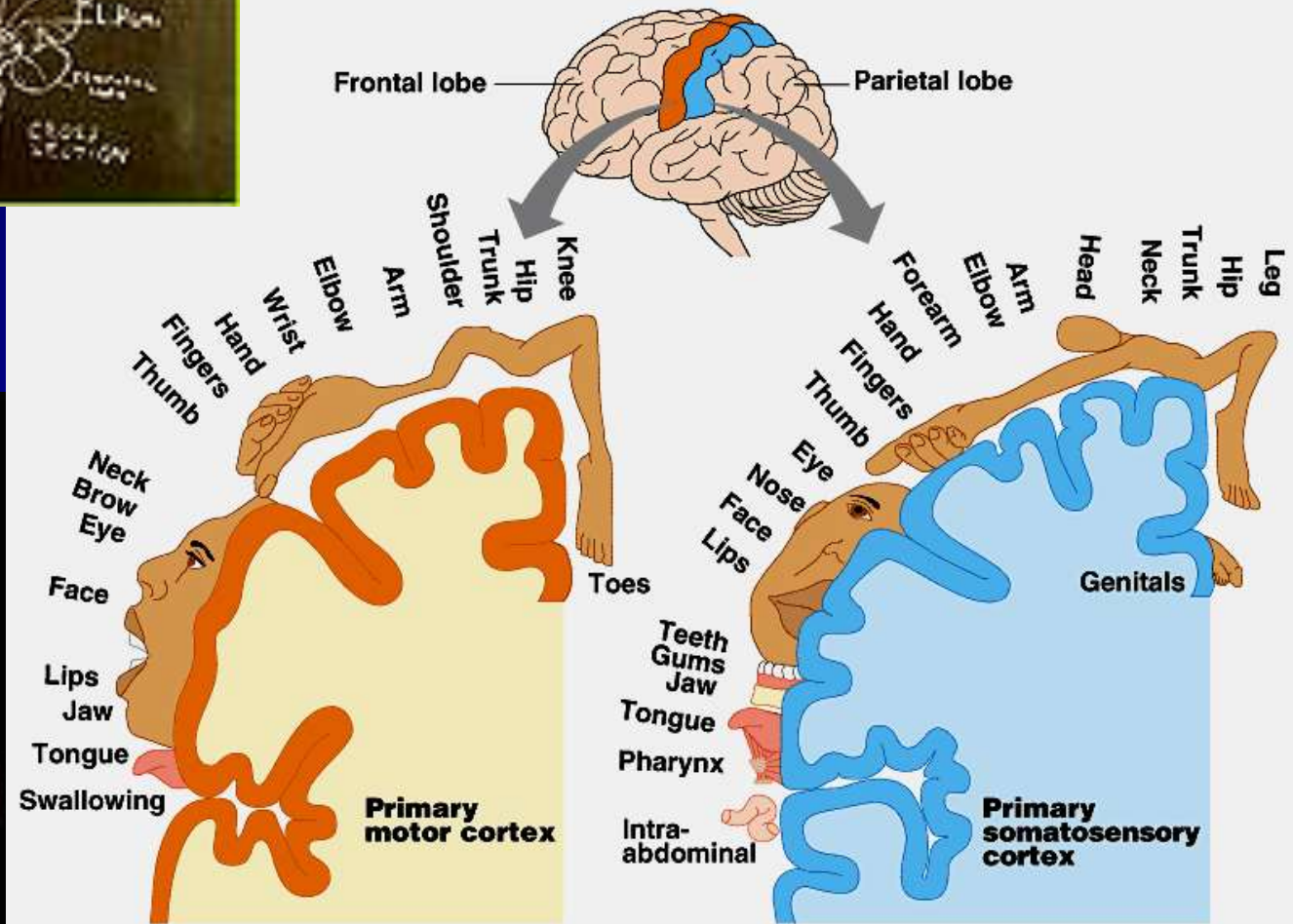
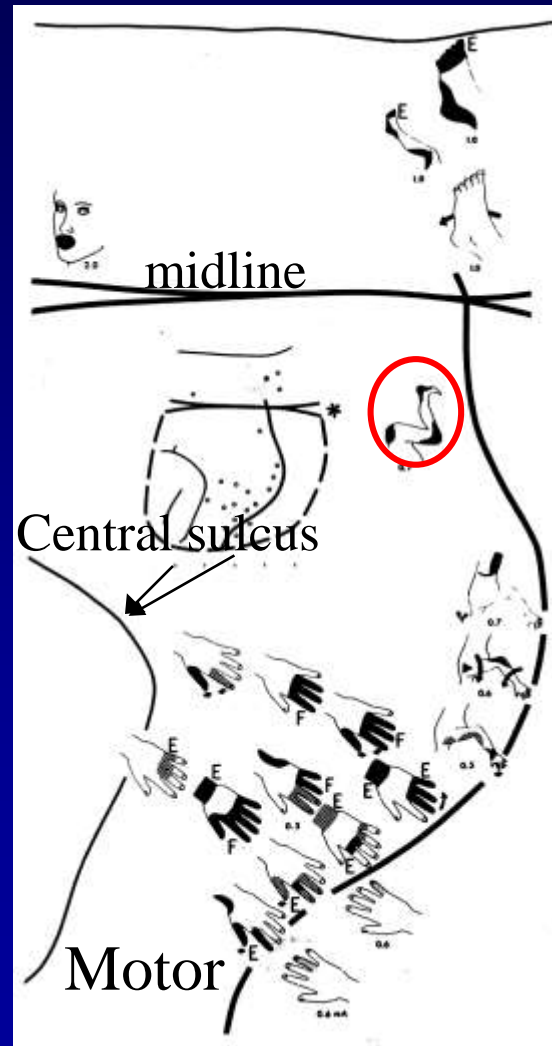
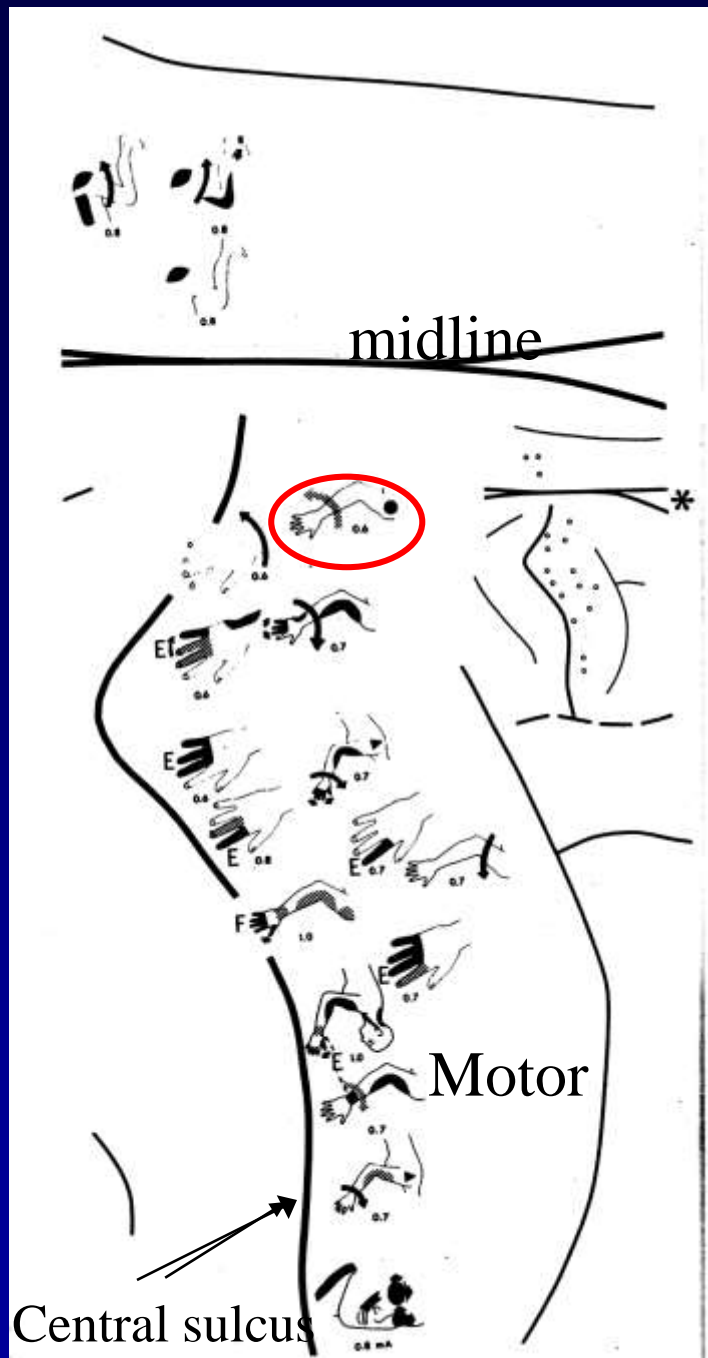
monopolar 60-cycle stimuli for 2 sec

# Neurophysiological aspects of motor cortex stimulation

Bipolar direct stimulation, 1ms, 50-60Hz, up to 20mA, for 1-4sec

# Neurophysiological aspects of motor cortex stimulation

midline

Motor

Central sulcus

**LEG REPRESENTATION**

- **1/3 medial surface**
- **2/3 lateral surface and**
- **in 27% the whole LE is on the lateral surface**

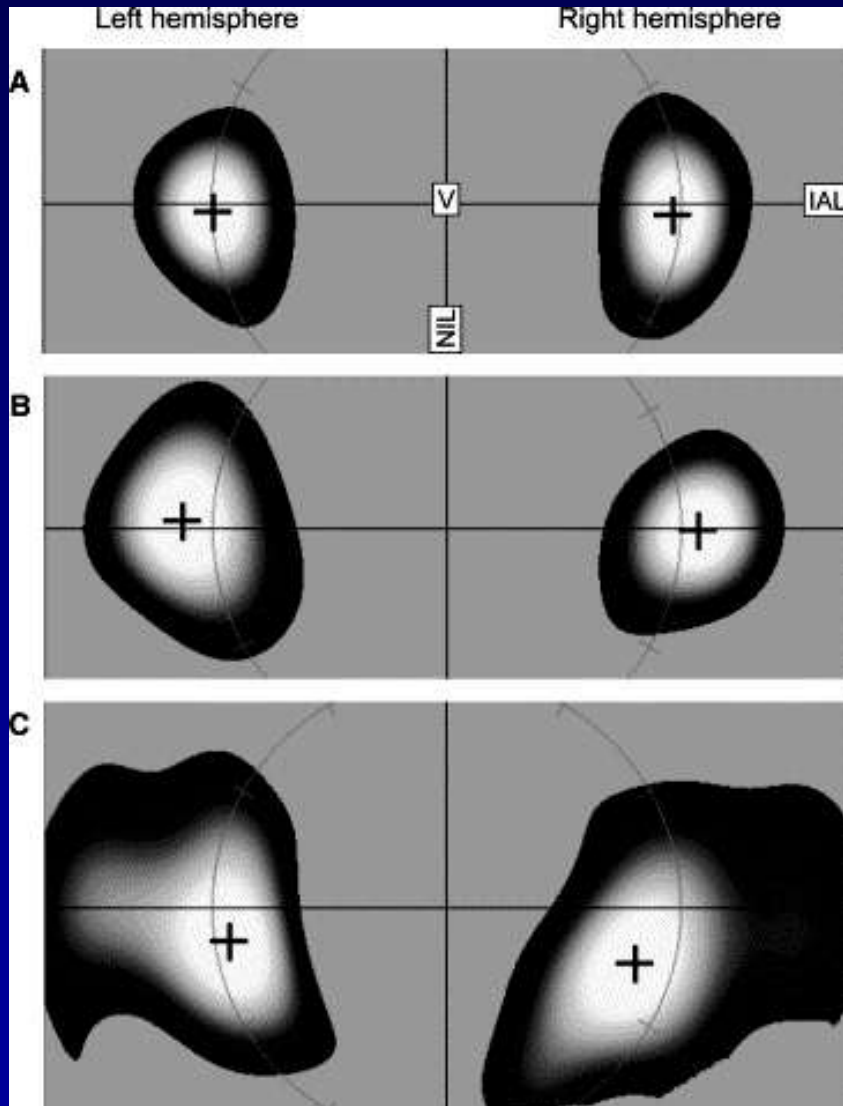
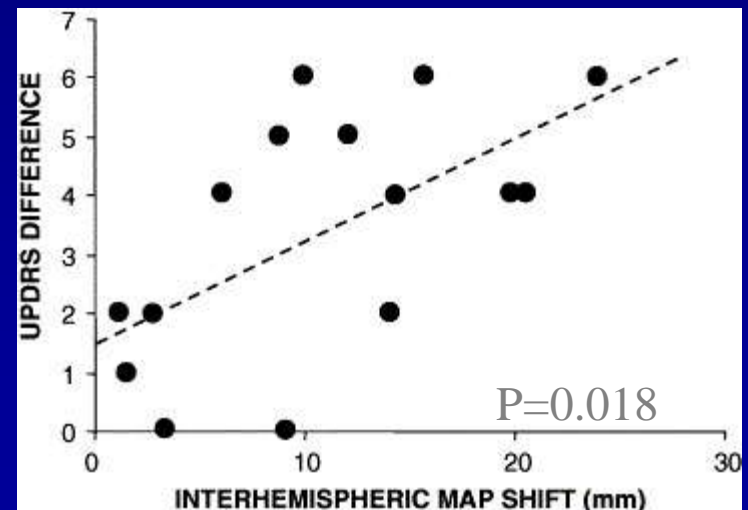
Woolsey et al, 1979

monopolar 60-cycle stimuli for 2 sec

# Neurophysiological aspects of motor cortex stimulation

Left hemisphere
Right hemisphere
A
B
C
V
IAL
NIL

## Motor cortex reorganization in Parkinson's disease

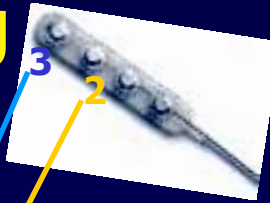
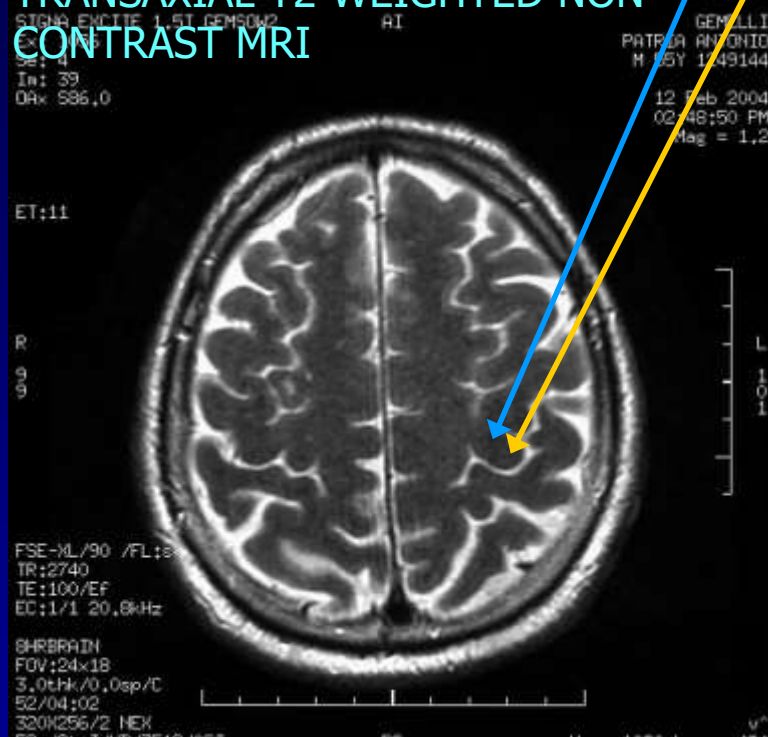
Thickbroom GW et al, 2006

- B and C: maps from PD subjects showing laterally displaced maps (B) and medially displaced maps with enlarged map area (C)
- A: map of APB in a control subject

# Motor Cortex Mapping

# Neurophysiological aspects of motor cortex stimulation

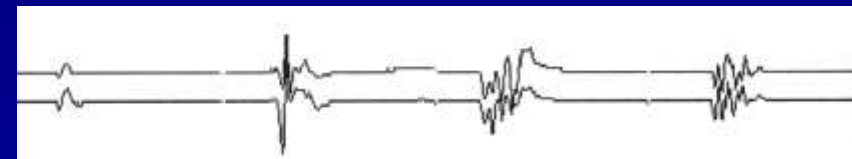
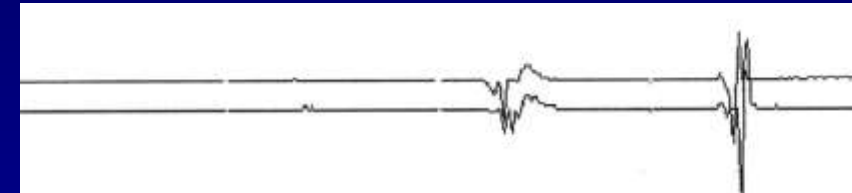
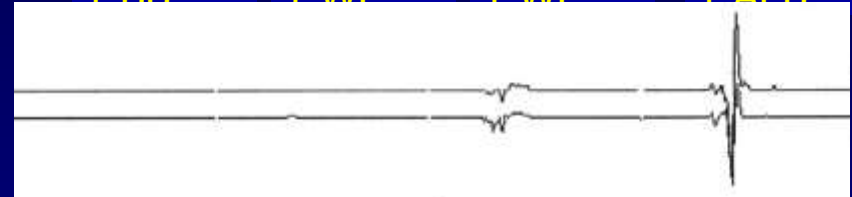
TRANSAXIAL T2-WEIGHTED NON CONTRAST MRI

3

2

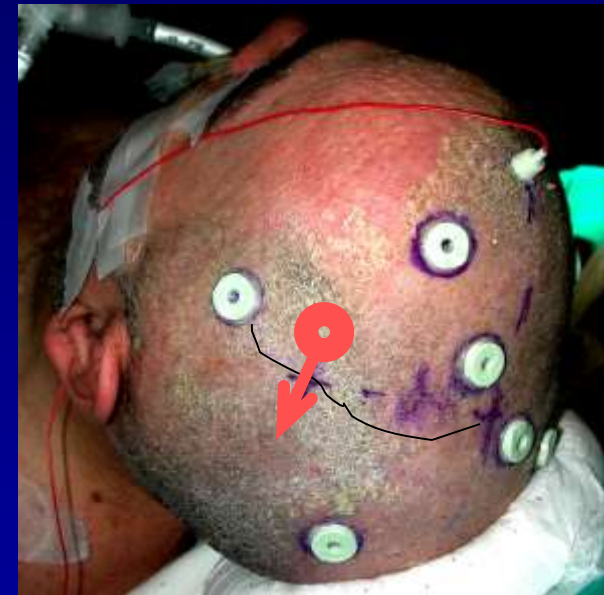
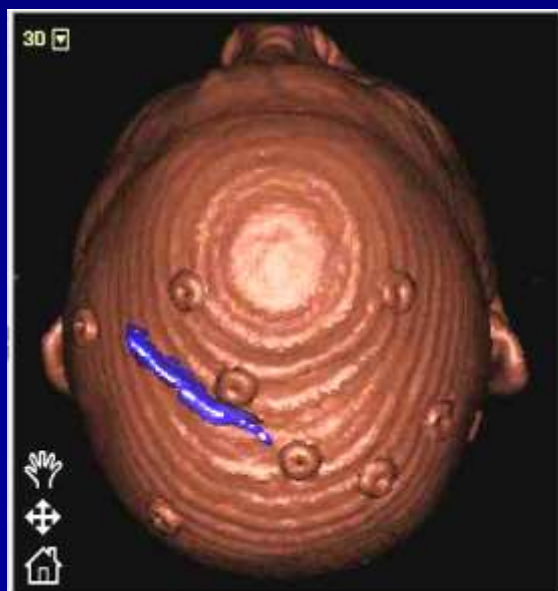
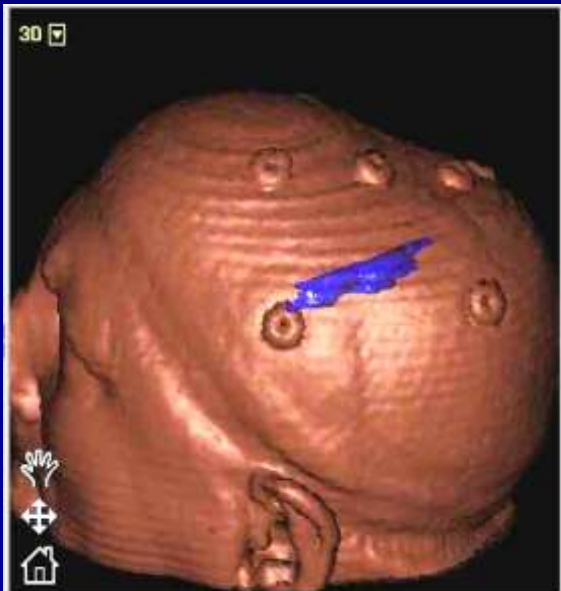
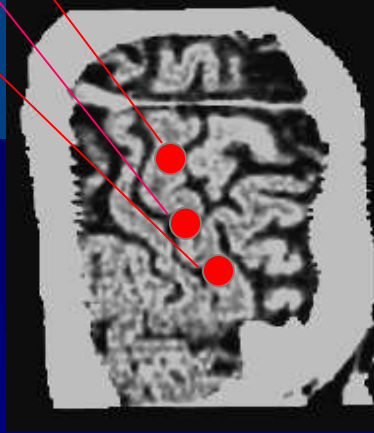
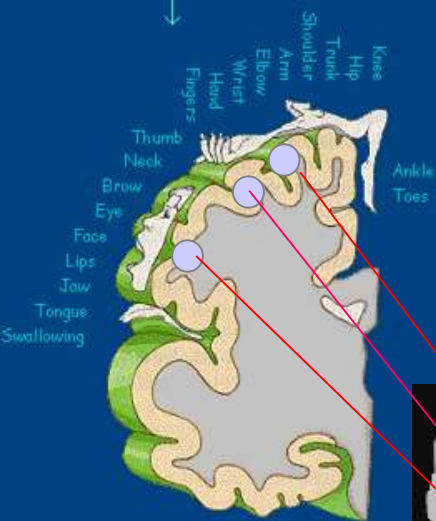
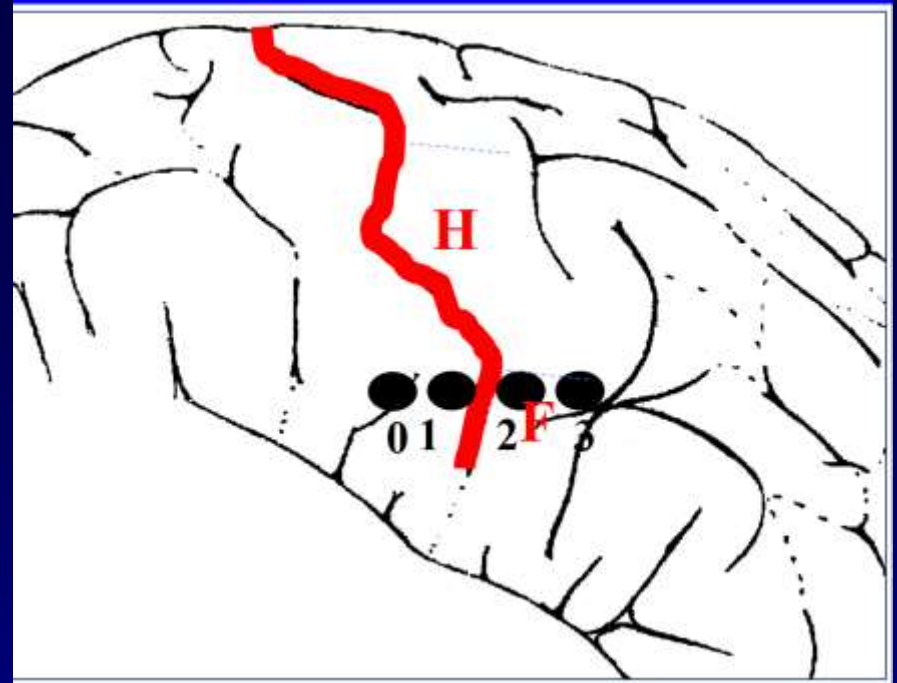
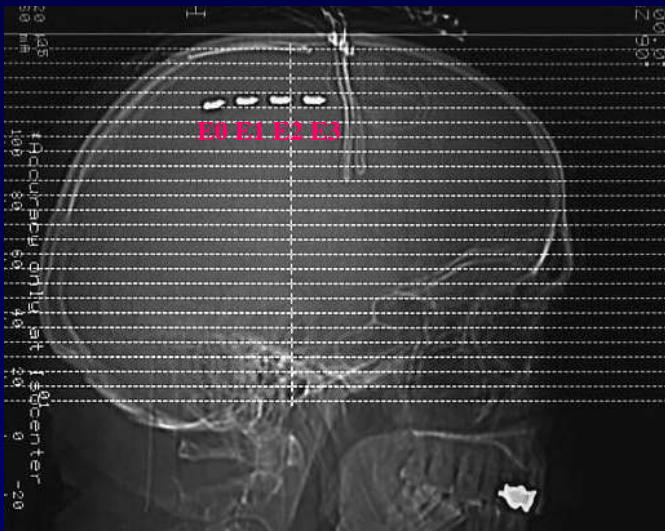
r BB | r WE | r WE | r APB

HAND

FOREARM

FOREARM

## MEPs

**Stimulation: cortical electrode (2+ 3-, train of 5 stimuli, 0.5 msec, ISI 4 msec, up to 20 mA, 2 Hz).**

**Recordings from muscle bellies with needle electrodes.**

# Motor cortex stimulation for pain relief: surgical planning

TIVA

**SEPs phase reversal**

**Electrical stimulation of the right median nerve at the wrist (0.5 ms, 23.3 mA, 4.7 Hz).**

**Stimulation: train of 5 stimuli, 0.5 msec, ISI 4 msec, 15 mA, 2trains/s).**

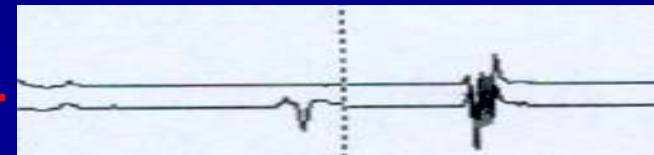
E0-FZ

E1-FZ

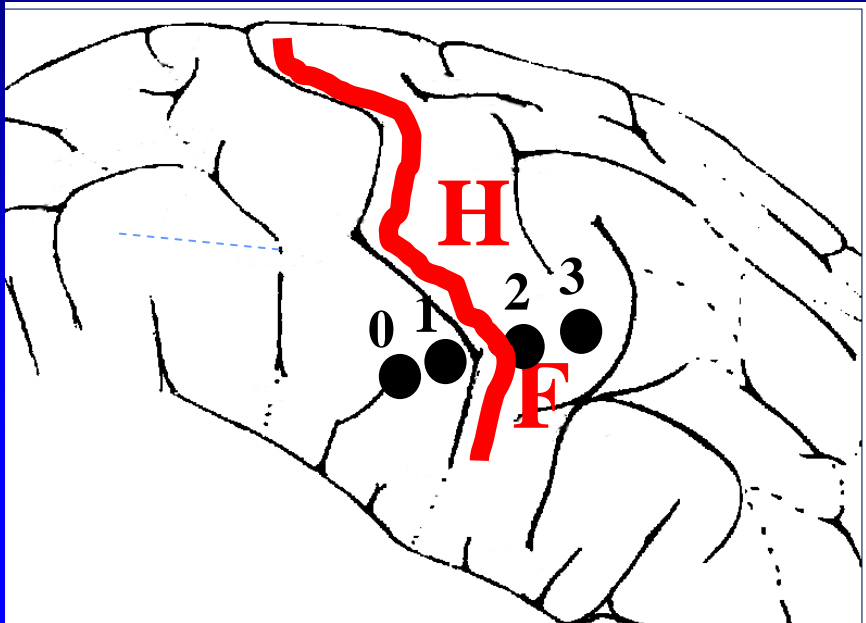
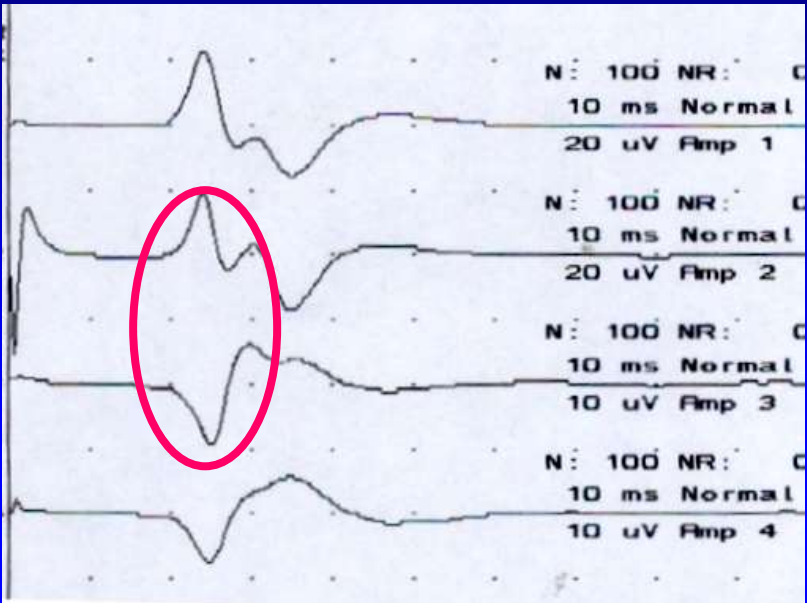
E2-FZ

E3-FZ

Rt BB

RtAPB

E1+E0-

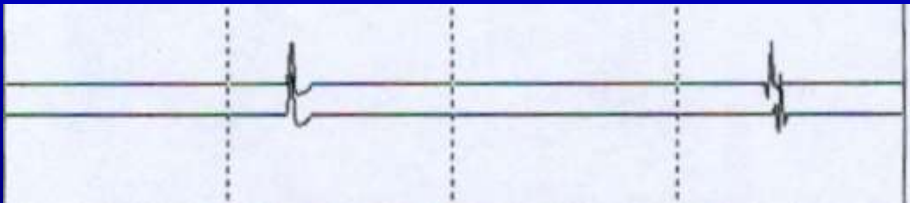
# rt facial post-herpetic neuralgia

E0-FZ
E1-FZ
E2-FZ
E3-FZ

**SEPs phase reversal**

**Electrical stimulation of the right median nerve at the wrist (0.5 ms, 23.3 mA, 4.7 Hz).**

**Motor mapping**

**Stimulation: train of 5 stimuli, 0.5 msec, ISI 4 msec, 15 mA, 2trains/s).**

E1+E0-

Rt BB Rt WE Rt WF Rt APB

# PROGNOSTIC FACTORS:
# Pharmacological tests

Regression analysis comparing % pain relief obtained with pharmacological tests and MCS

Yamamoto et al, Pain, 1997

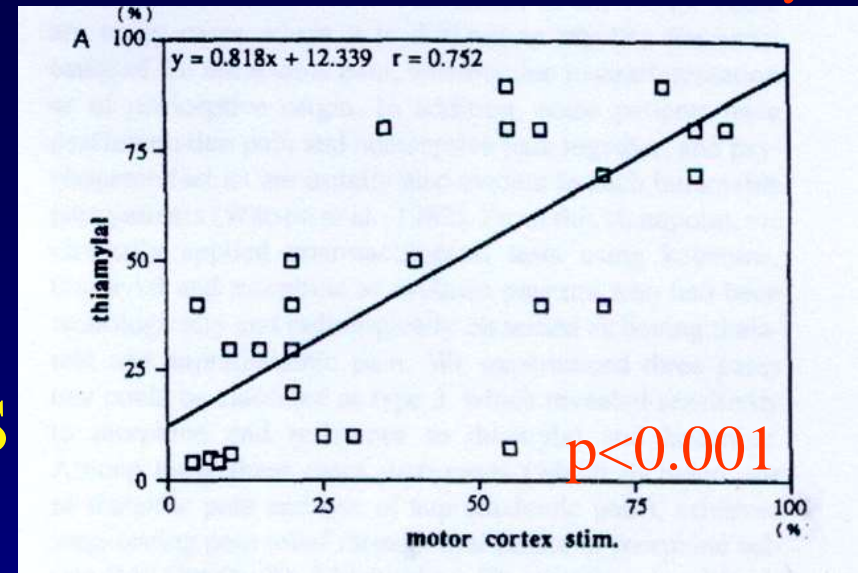
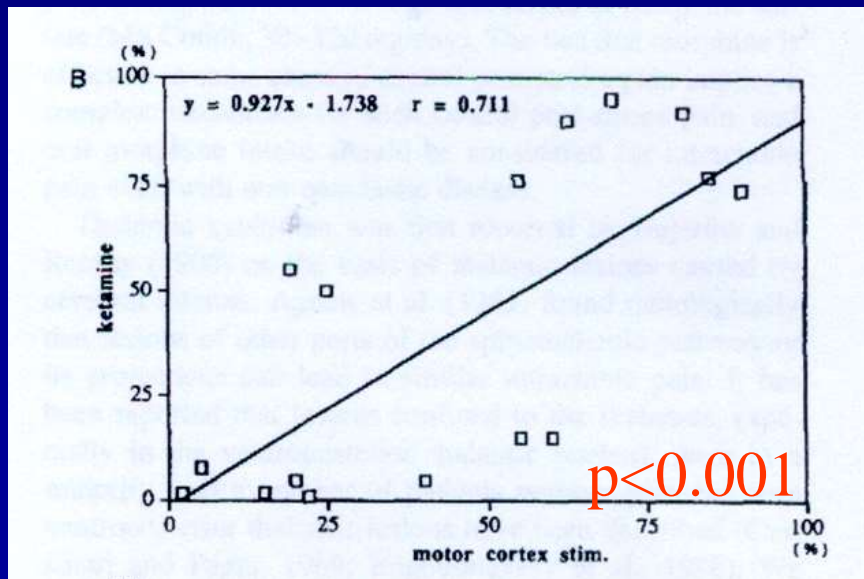
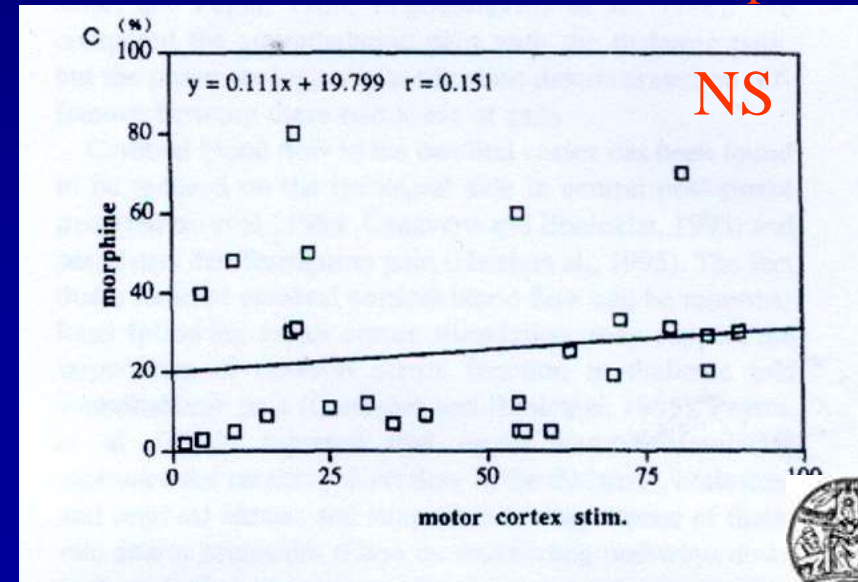
thiamytal

p<0.001

ketamine

p<0.001

morphine

NS

# PROGNOSTIC FACTORS: rTMS

- Repetitive Transcranial Magnetic Stimulation (rTMS) of the motor cortex corresponding to the painful zone
  - Intensity of stimulation : 80% of rest motor threshold
  - Frequency : 10 Hz
  - Train duration : 10 seconds
  - Intertrain interval : 1 minute
  - Number of trains : 20
  - Duration of one session : 20’

- Sham rTMS : Same protocol without any magnetic shock delivered (double blind)

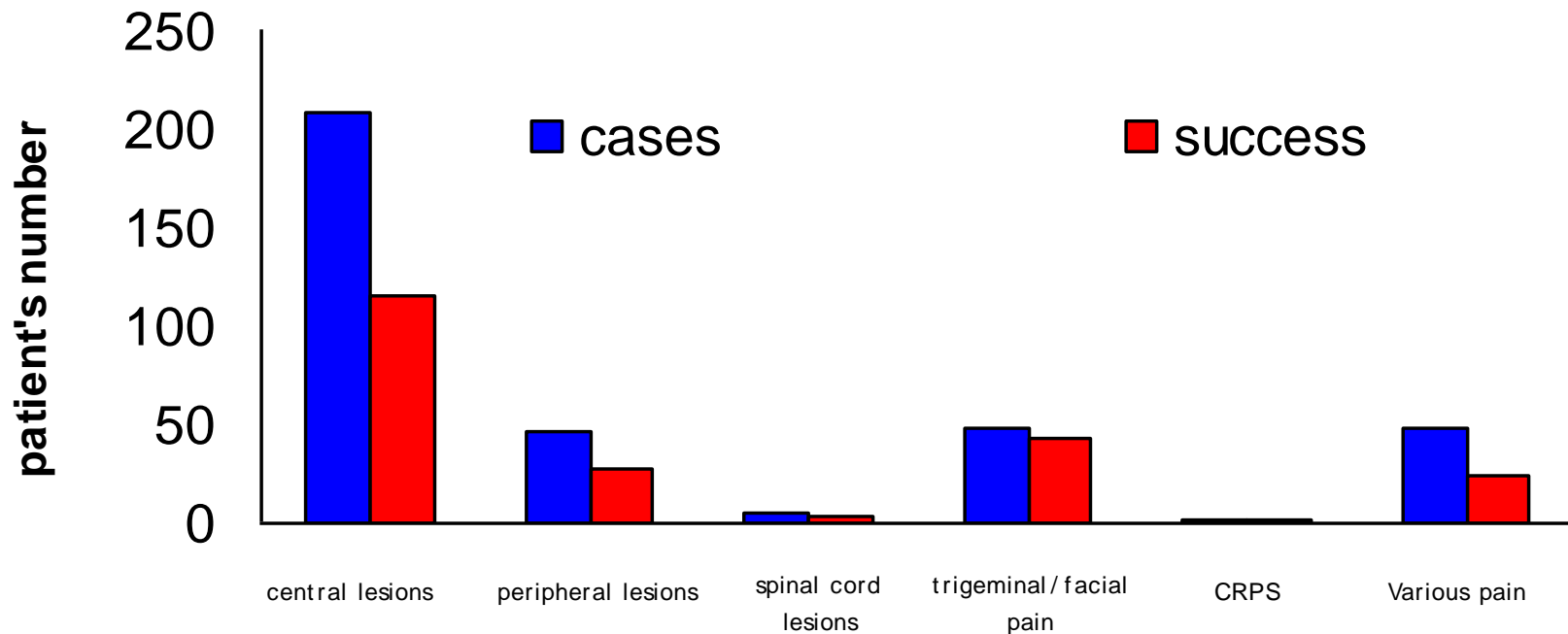
# CHRONIC MOTOR CORTEX STIMULATION FOR PAIN: RESULTS

## *Results from the literature 2005*

patient's number

250
200
150
100
50
0

cases
success

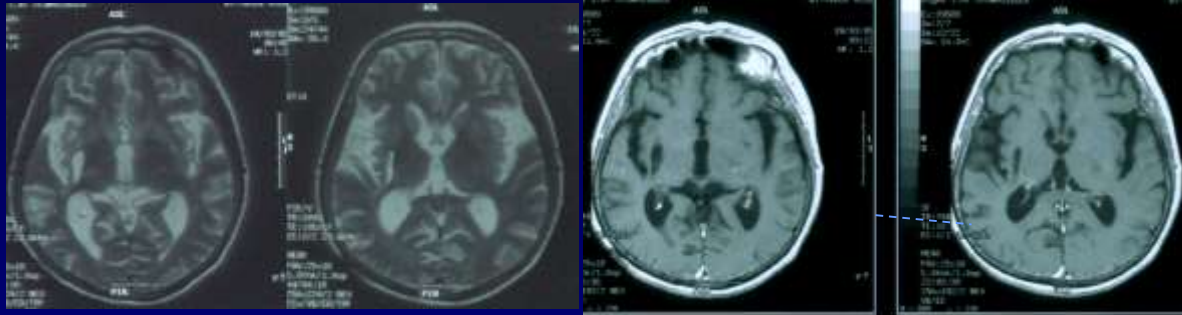
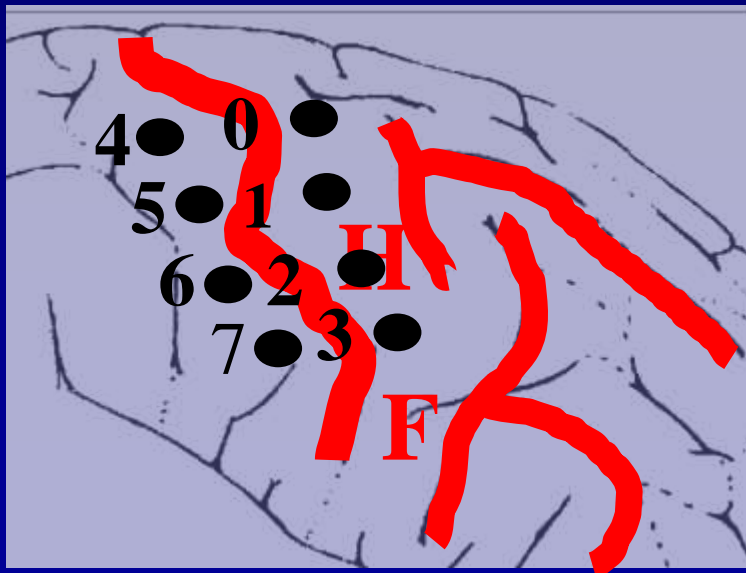
central lesions
peripheral lesions
spinal cord lesions
trigeminal / facial pain
CRPS
Various pain

# Motor cortex stimulation for pain relief: personal results

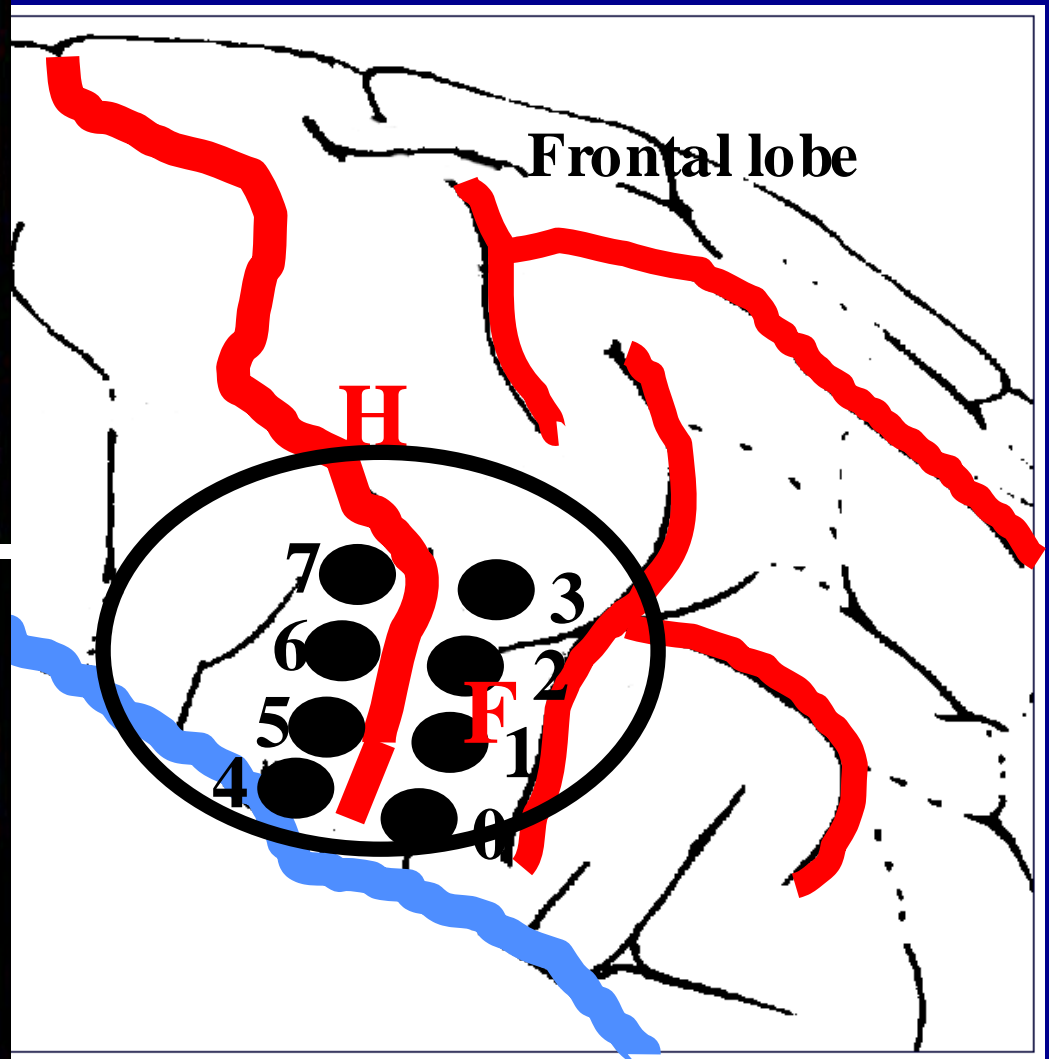
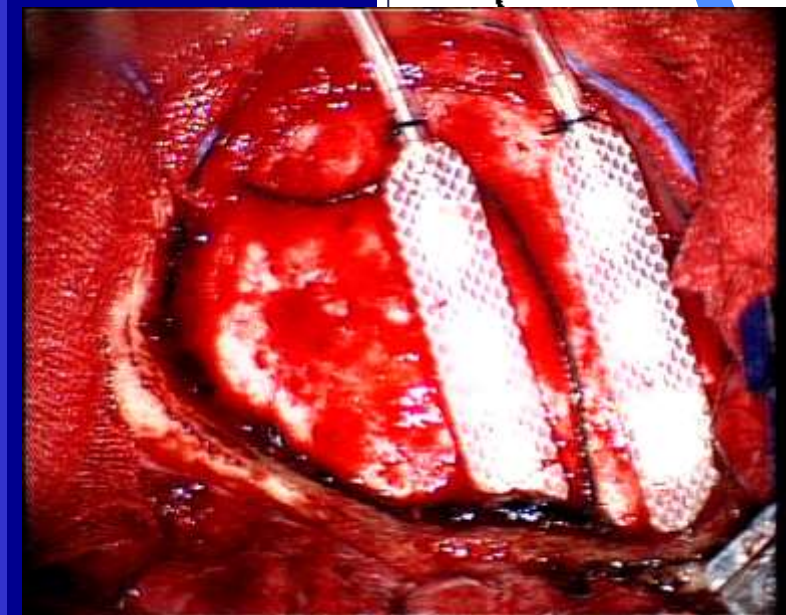
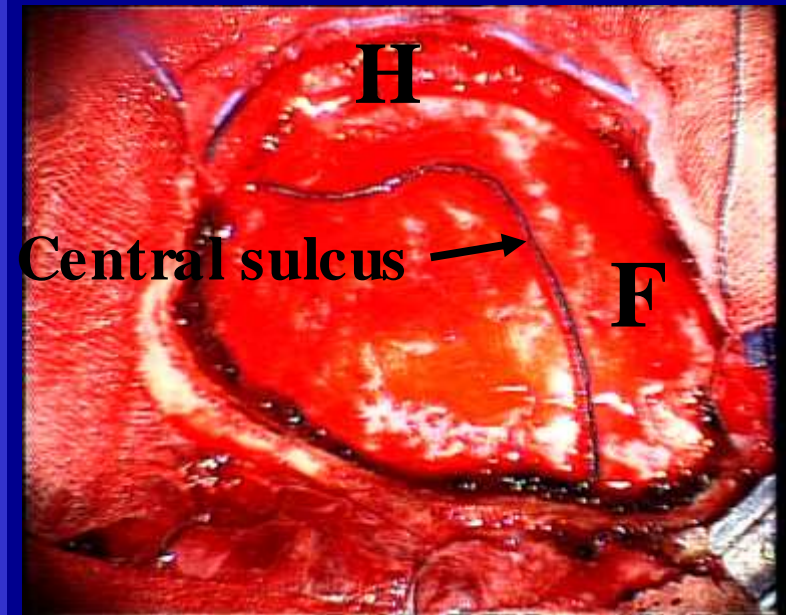
## Long term pain relief: 13 patients*

**(mean FU: 24 months)**

- **>/= 40% : 3 patients (23%)**
- **0% : 10 patients (77%)**

***1 patient had an epileptic seizure at the very first programming and required the system removal**

# Motor cortex stimulation for pain: the future (?)

Left upper extremity central deafferentation pain

**Stim: 0- 7- 3+ 4+; 80Hz, 120 usec, 3.5V, during daytime**

# Motor cortex stimulation for pain: the future (?)

Left facial deafferentation pain

# Motor cortex stimulation for pain relief

## Possible mechanisms of action

Tsubokawa et al, Acta Neurochirurgica, 1991

**Black arrows:inhibition; white arrows: excitation**

# PET scan CBF increase

Garcia-Larrea et al,
Pain, 1999

Thalamus

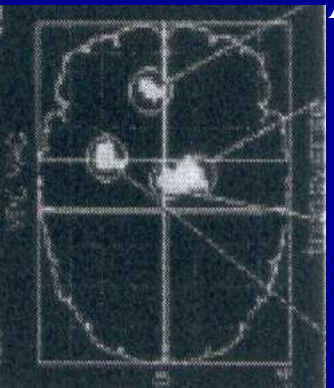
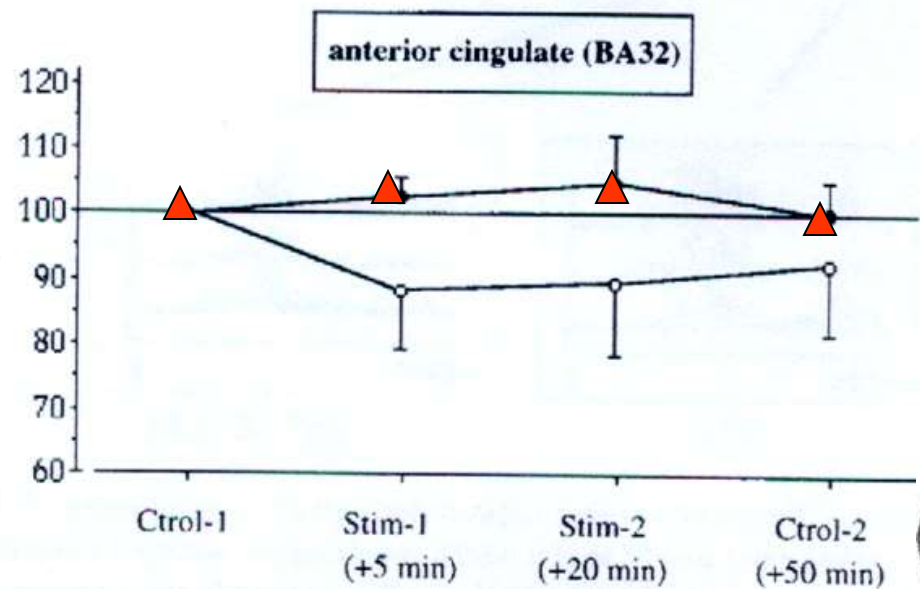
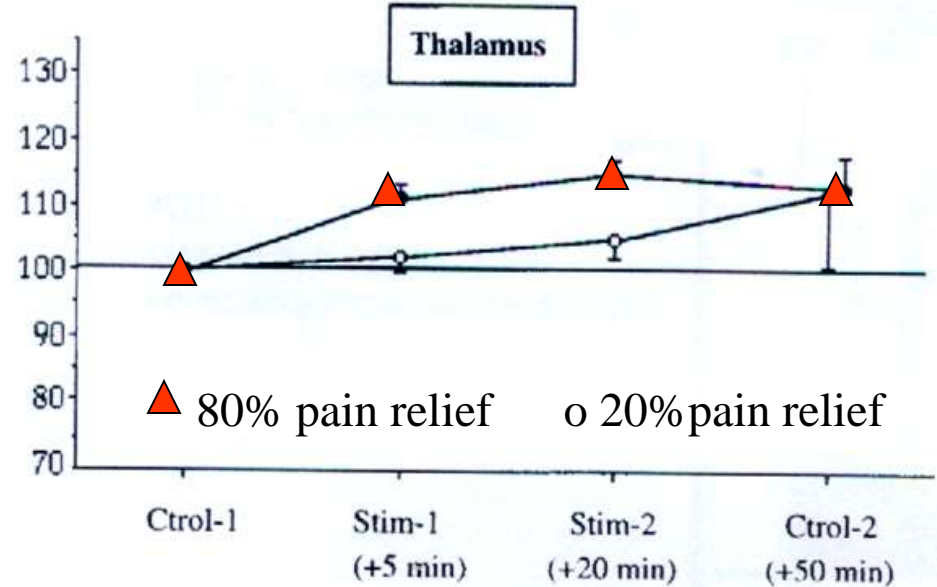
130
120
110
100
90
80
70

80% pain relief o 20%pain relief

Ctrol-1
Stim-1 (+5 min)
Stim-2 (+20 min)
Ctrol-2 (+50 min)

anterior cingulate (BA32)

120
110
100
90
80
70
60

Ctrol-1
Stim-1 (+5 min)
Stim-2 (+20 min)
Ctrol-2 (+50 min)

## **PET scan CBF increase:** Saitoh et al, J Neurosurg, 2004

**A: lt rectus gyrus**

**B: lt sup frontal gyrus**

**C: lt thalamus**

**D: rt sup temporal gyrus**

**E: lt mid occipital gyrus**

rCBF (ml/100g/min)

60

50

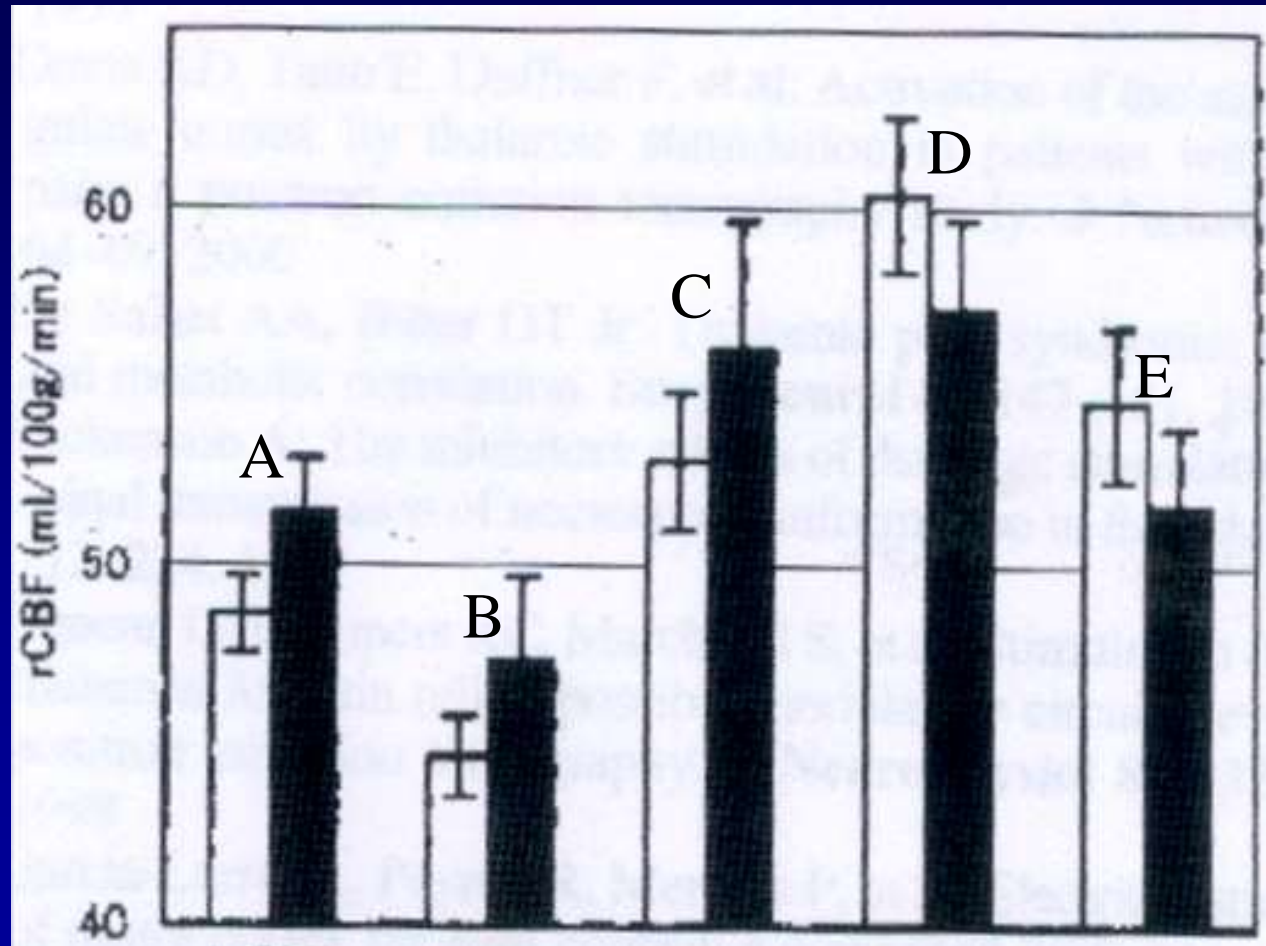
40

A

B

C

D

E

White bars: pain; black bars: rt MCS and pain relief

# Nociceptive flexion reflexes

on off on off

Patient : A.M.
left cortex stimulation

nVs

RIII :
stimulation : right sural
recording: right biceps femoris

NOCICEPTIVE FLEXION
REFLEXES DURING
MOTOR CORTEX STIMULATION

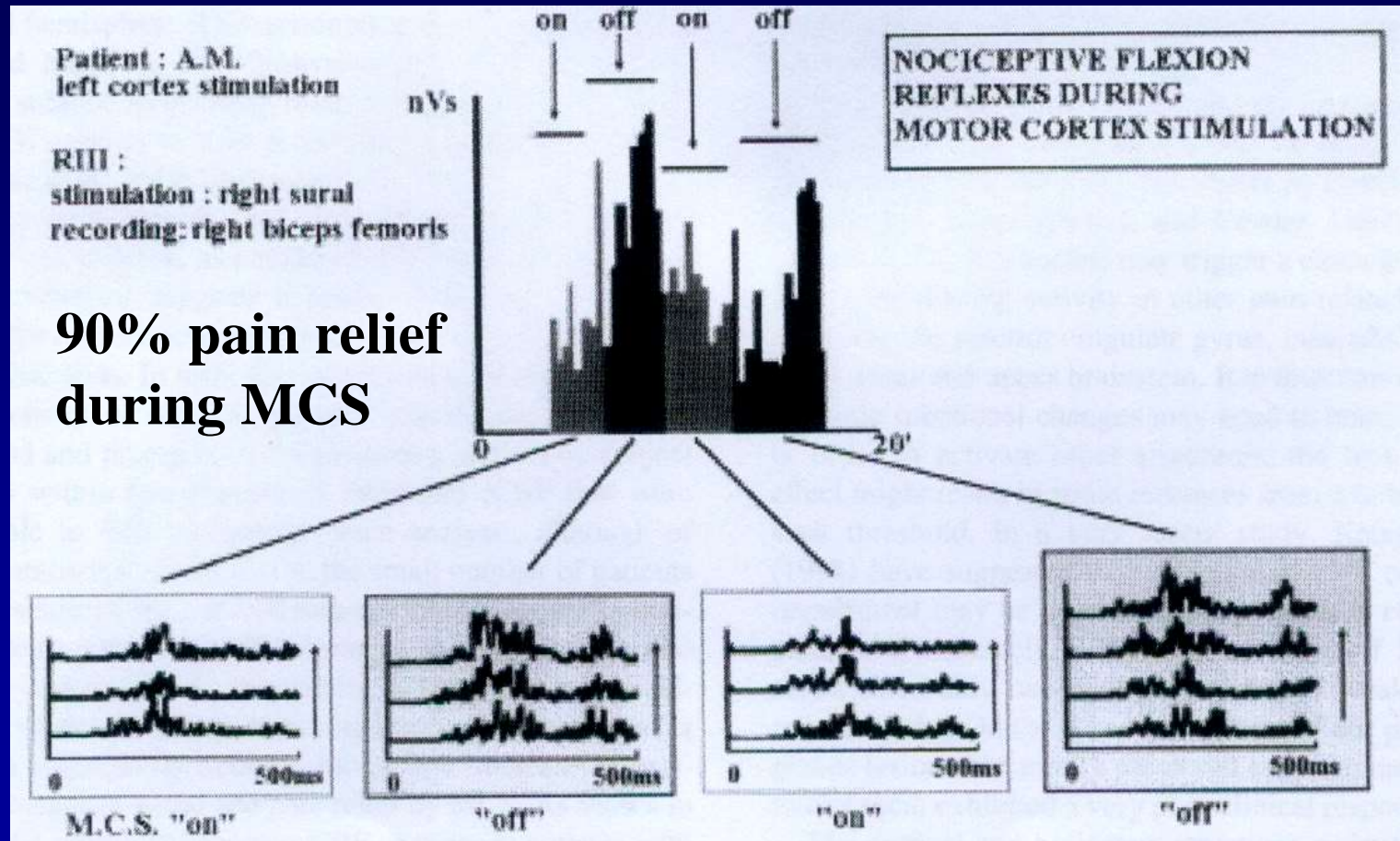
**90% pain relief during MCS**

0 20'

0 500ms M.C.S. "on"

0 500ms "off"

0 500ms "on"

0 500ms "off"

Garcia-Larrea et al, Pain, 1999

# MCS decreases spinal dorsal horn neurons activity in rats

Senapati et al, Brain Res,2005

**MCS produced significant inhibition of wide dynamic range dorsal horn neurons to high intensity mechanical painful stimuli but not to innocuous stimuli**

A Site of stimulation

M1 M2 M1 S1FL Cg1 Cg2

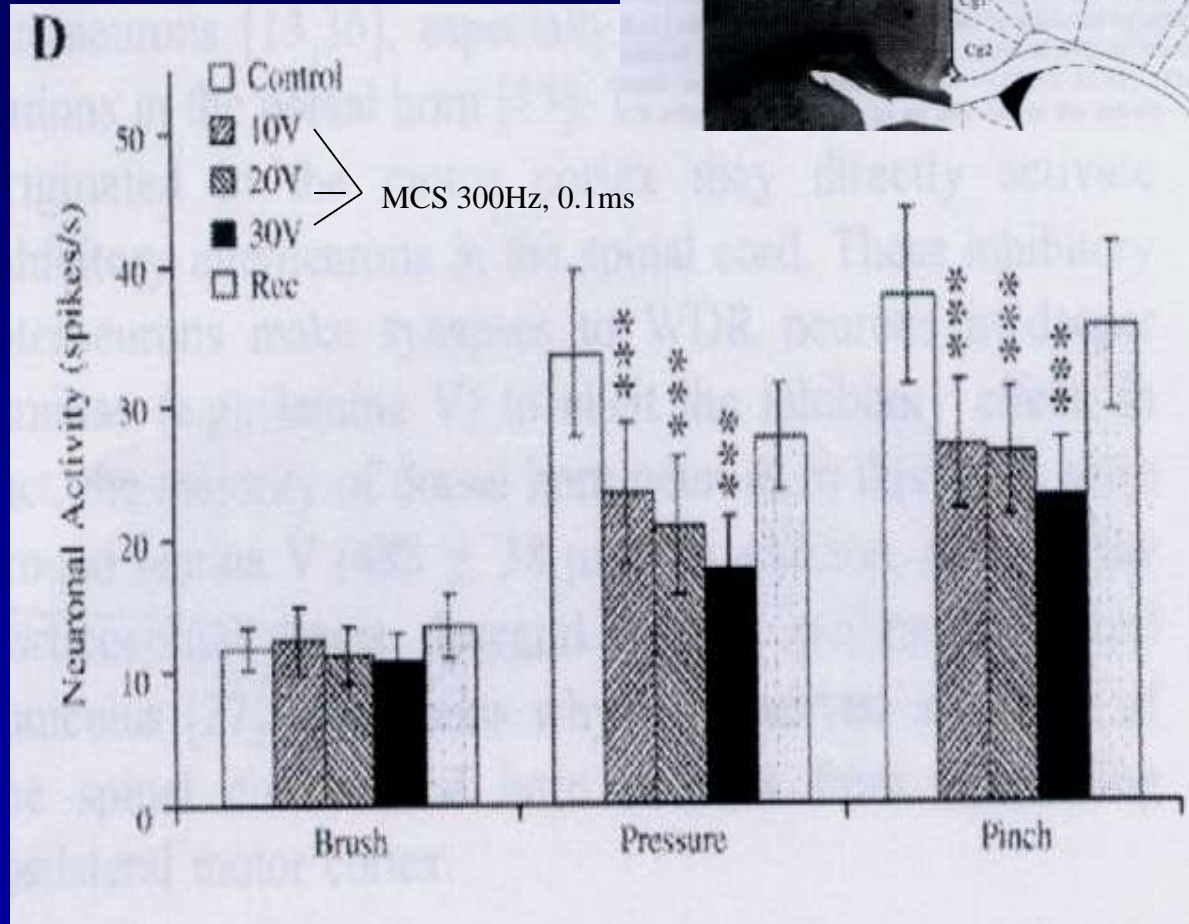
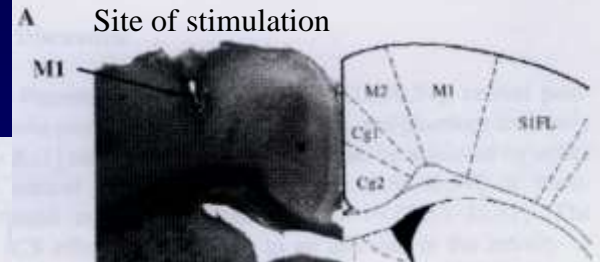
D

Control
10V
20V
30V
Rec

MCS 300Hz, 0.1ms

Neuronal Activity (spikes/s)

0 10 20 30 40 50

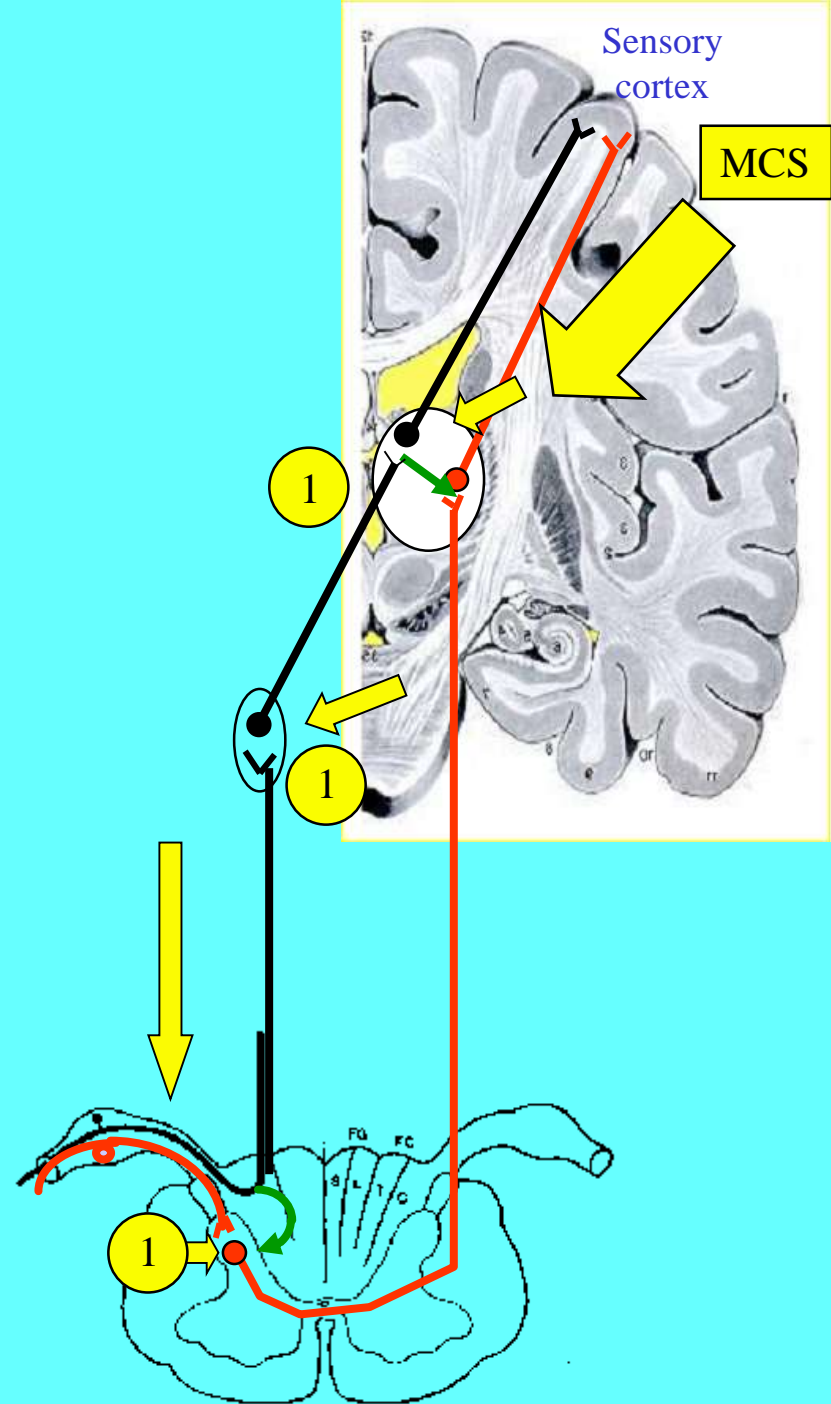
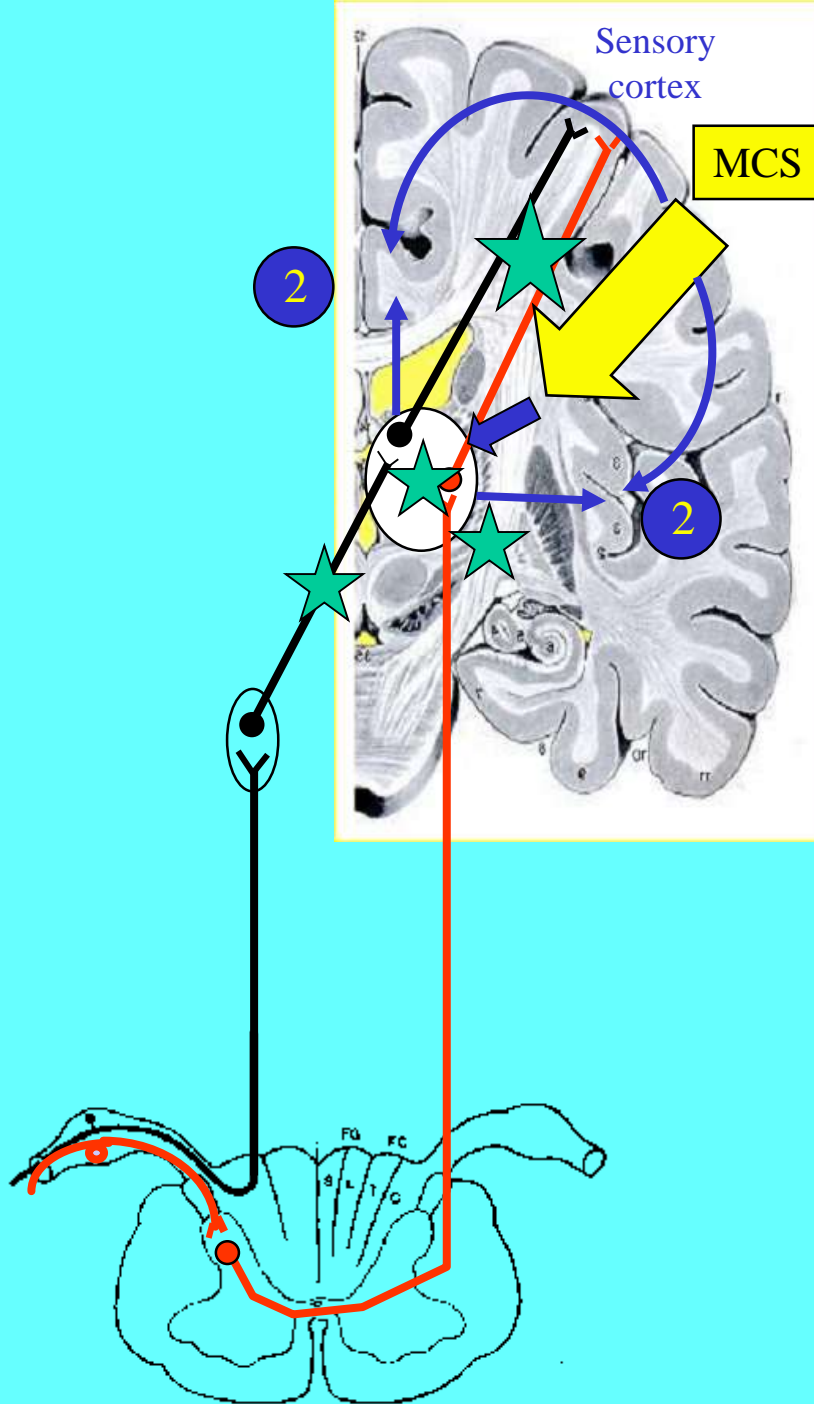
Brush Pressure Pinch

**MCS may act**
**by reinforcing the control of non-nociceptive sensory inputs (black) on nociceptive systems (red) at the level of the thalamus, dorsal column nuclei and spinal cord.**

- ❑ MCS-induced pain relief is associated with an improved sensory discrimination within the painful zone suggesting that MCS acts on somatosensory pathways and sensory processing
- ❑ In experimental models of deafferentation pain, MCS reduce the hyperactivity in VPL and DCN
- ❑ PET studies exhibited a major involvement of the thalamus and the brainstem
- ❑ MCS induces an attenuation of RIII reflex suggesting that MCS could exert an inhibitory control on spinal cord segments.
- ❑ Relative preservation of the pyramidal tract and somatosensory pathways seems to be essential for a good clinical result.

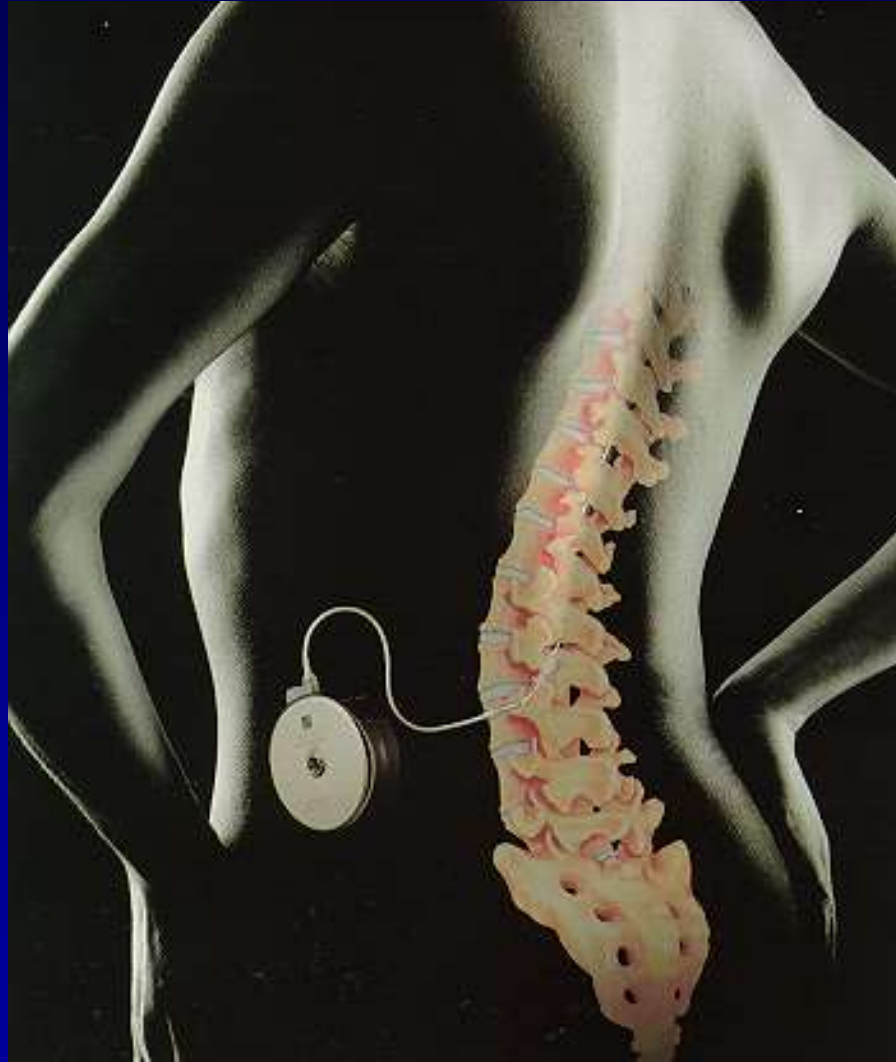
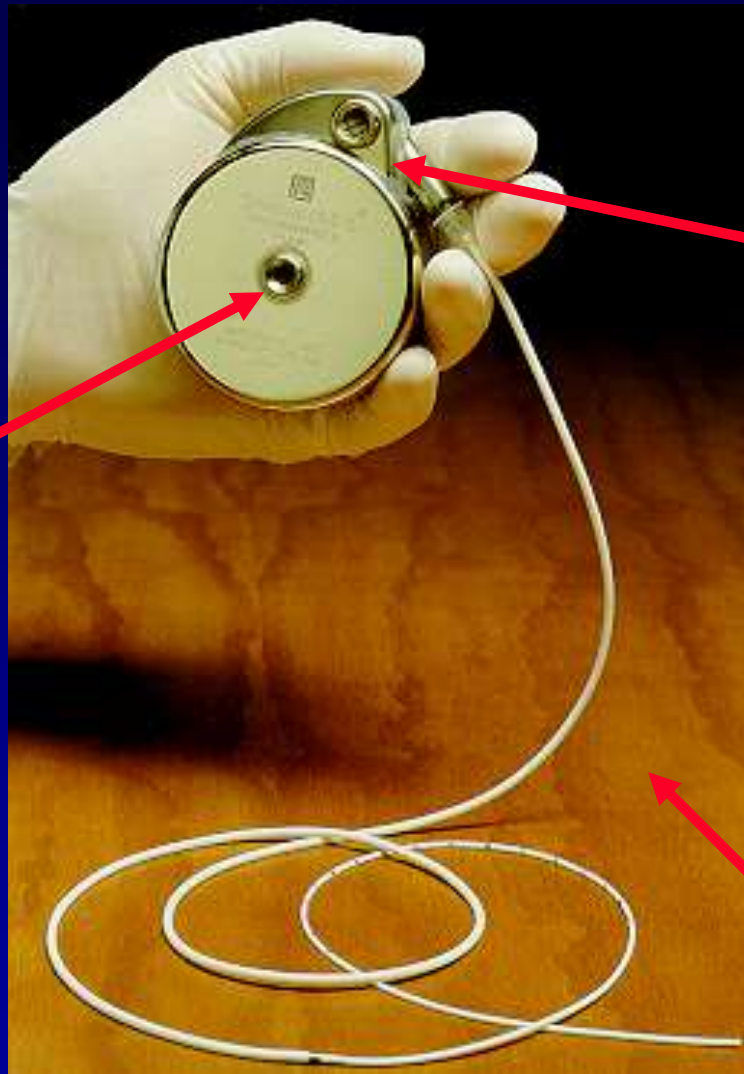
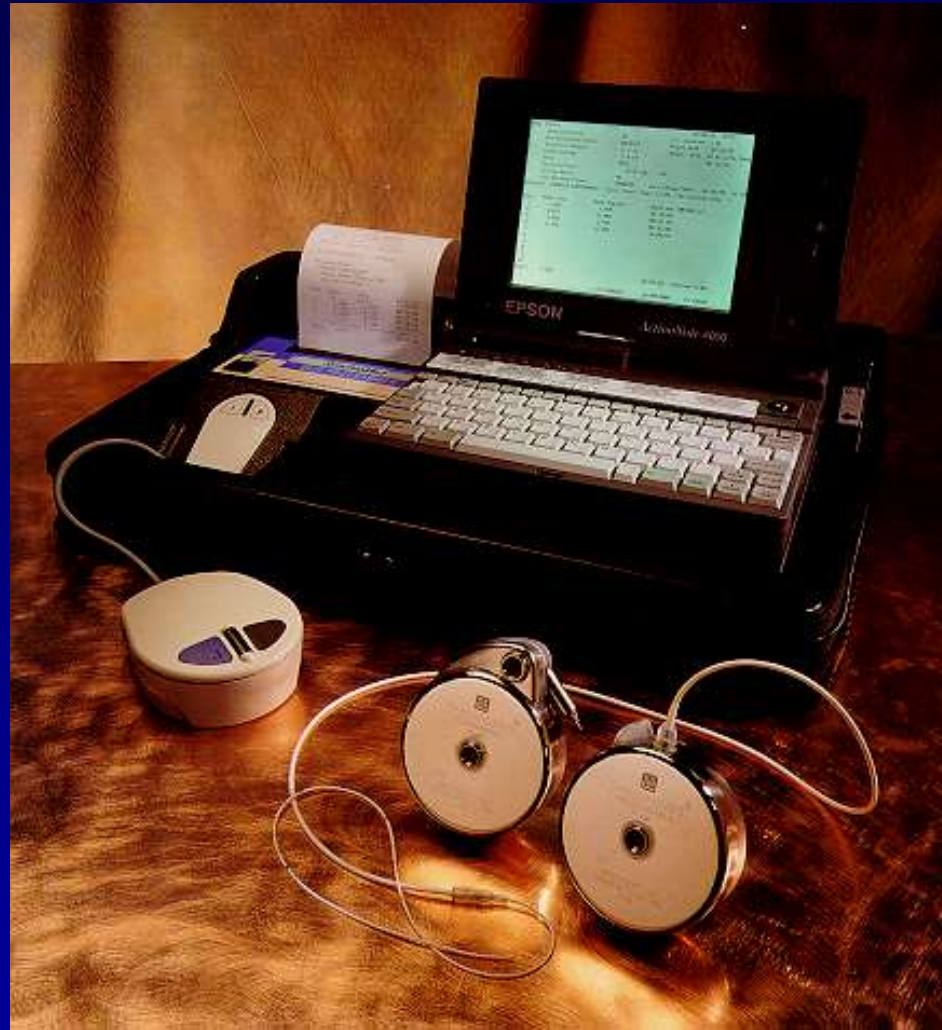
Sensory cortex

MCS

2

2

**MCS may reduce the emotional component of chronic pain by activating the anterior cingulate cortex and the anterior insula** which are implicated in both the cognitive and the affective integration of pain stimuli (PET studies, Lyon)

Action of MCS on :
-Sensory cortex ?
-Endorphine sites in the brainstem ?

# Infusione intratecale di farmaci

Direct connection to the catheter
To fill the reservoir
Spinal catheter

# Intrathecal infusion of drugs

- Selected patients;
- Opioids, local anesthetic, nonopioids acting on adrenergic or GABA recectors;
- No neurotoxicity after opioids infusion;
- Development of tolerance;
- New target: Polyanalgesia*

*Rainov et al (2001)
Deer et al.(2002)

# Dolore cronico benigno: il razionale della terapia chirurgica

Trattamento meno invasivo — Trattamento più invasivo

continuum

Approcci psicologici e fisici

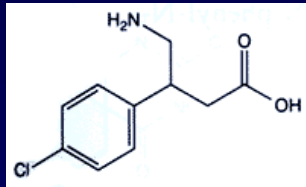
Farmaci topici

Farmaci orali

Farmaci per iniezione

Blocchi antalgici

***Neuromodulazione***

***Interventi demolitivi***

# Baclofen intratecale nel trattamento della spasticità

# SPASTICITA’
## Definizione clinica

- **Ipertonia muscolare riflessa**
- **Spasmi spontanei e provocati**
- **Esaltazione dei riflessi osteotendinei**
- **Riflessi di difesa**

accompagnati da**:**

- **deficit del movimento volontario**

# BACLOFEN
## GABA-B agonista

Agisce a livello spinale riducendo l’entrata di Ca++ nelle terminazioni presinaptiche e ad alte concentrazioni, diminuisce l’ eccitabilità neuronale a livello postsinaptico

# BACLOFEN
## GABA-B agonista

Deprime i riflessi mono e polisinaptici:

**diminuisce ipertono e spasmi**

# BACLOFEN
## GABA-B agonista

Passa con difficoltà la barriera ematoencefalica

Dopo somministrazione sistemica:

$[Baclofen_{plasma}]:[Baclofen_{CSF}] = 10:1$

# BACLOFEN
## GABA-B agonista

Passa con difficoltà la barriera ematoencefalica

Dopo somministrazione liquorale:

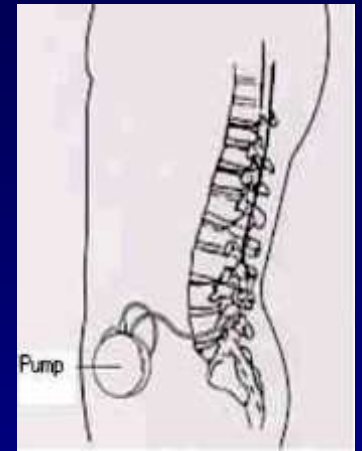
milligrammi diventano microgrammi

# BACLOFEN INTRATECALE

## Indicazioni (Penn e Kroin,1984)

- spasticità spinale
- spasticità severa
- spasmi in flessione
- preferibilmente agli arti inferiori
- risposta positiva al bolo test
- adulti

# SURGICAL TECHNIQUE:

- Positive response to IT bolus
- General anesthesia, peroperative antibiotics, lateral position
- Insertion of the spinal catheter slightly lateral to the spinous process with an oblique advancement in the lumbar intrathecal space
- The catheter is then threaded into the mid-high thoracic region
- An electronic continous infusion pump is placed within the lower abdominal wall in a suprafascial pocket

# BACLOFEN INTRATECALE: spasticità spinale
## Letteratura 1991-2001

- Sahuquillo, Acta Neurochir, 1991
- Coffey, J Neurosurg, 1993
- Nance, Can J Neurol Sci, 1995
- Azouvi, Arch Phys Med Rehabil, 1996
- Ordia, J Neurosurg, 1996
- Middel, J Neurol Neurosurg Psych, 1997
- Lazorthes, Neurochirurgie,1998
- Burns, Spinal Cord,2001

# BACLOFEN INTRATECALE: spasticità spinale
## Letteratura 1991-2001

**281 PAZIENTI**

Follow up medio: 12-48 mesi

Dosaggio medio: 193-405 ugr/die

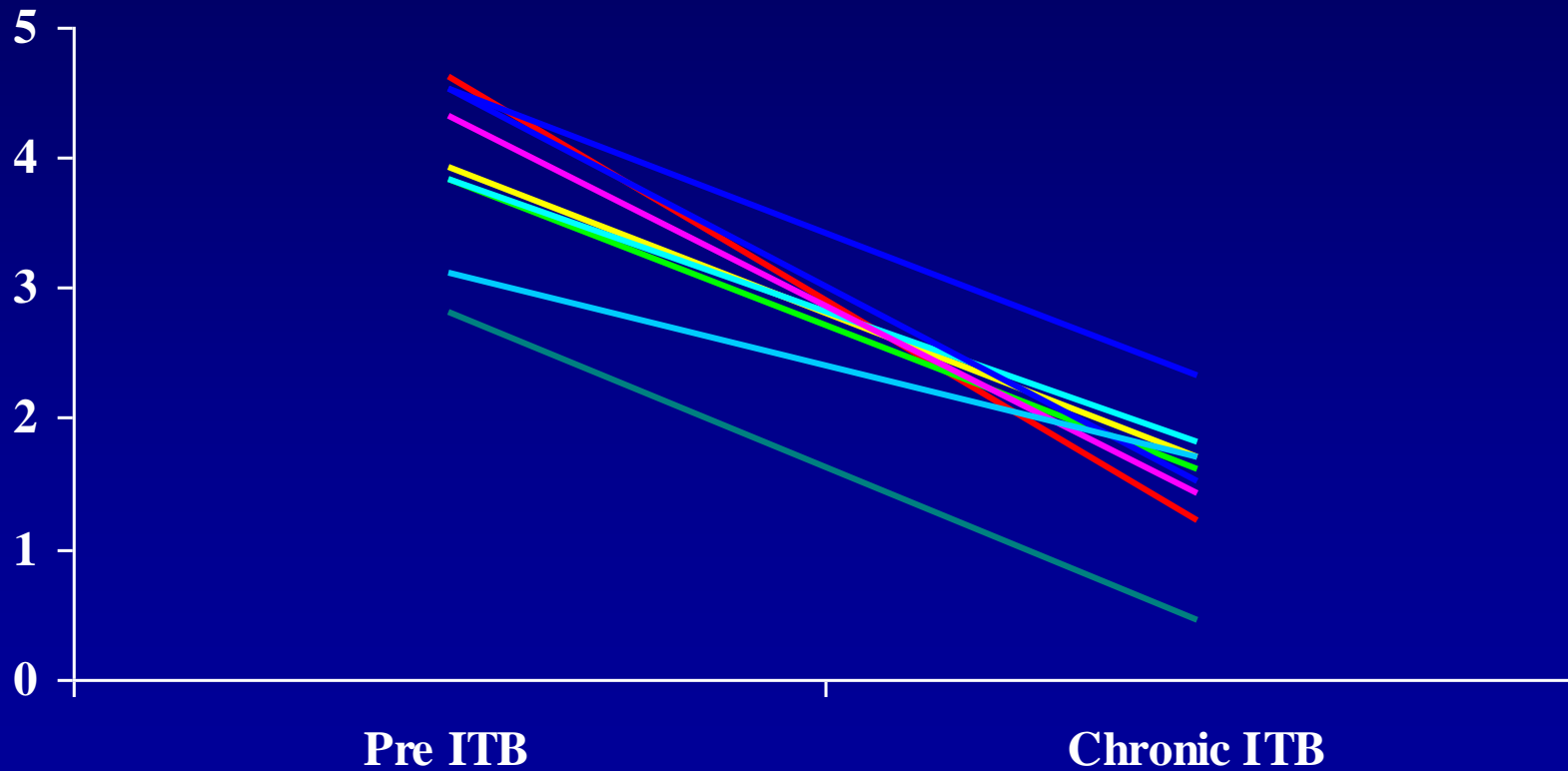
# BACLOFEN INTRATECALE
## Valutazione dei risultati

### Al bolo test

- scala di Ashworth (ipertono)
- scala di Penn (spasmi)

### A distanza

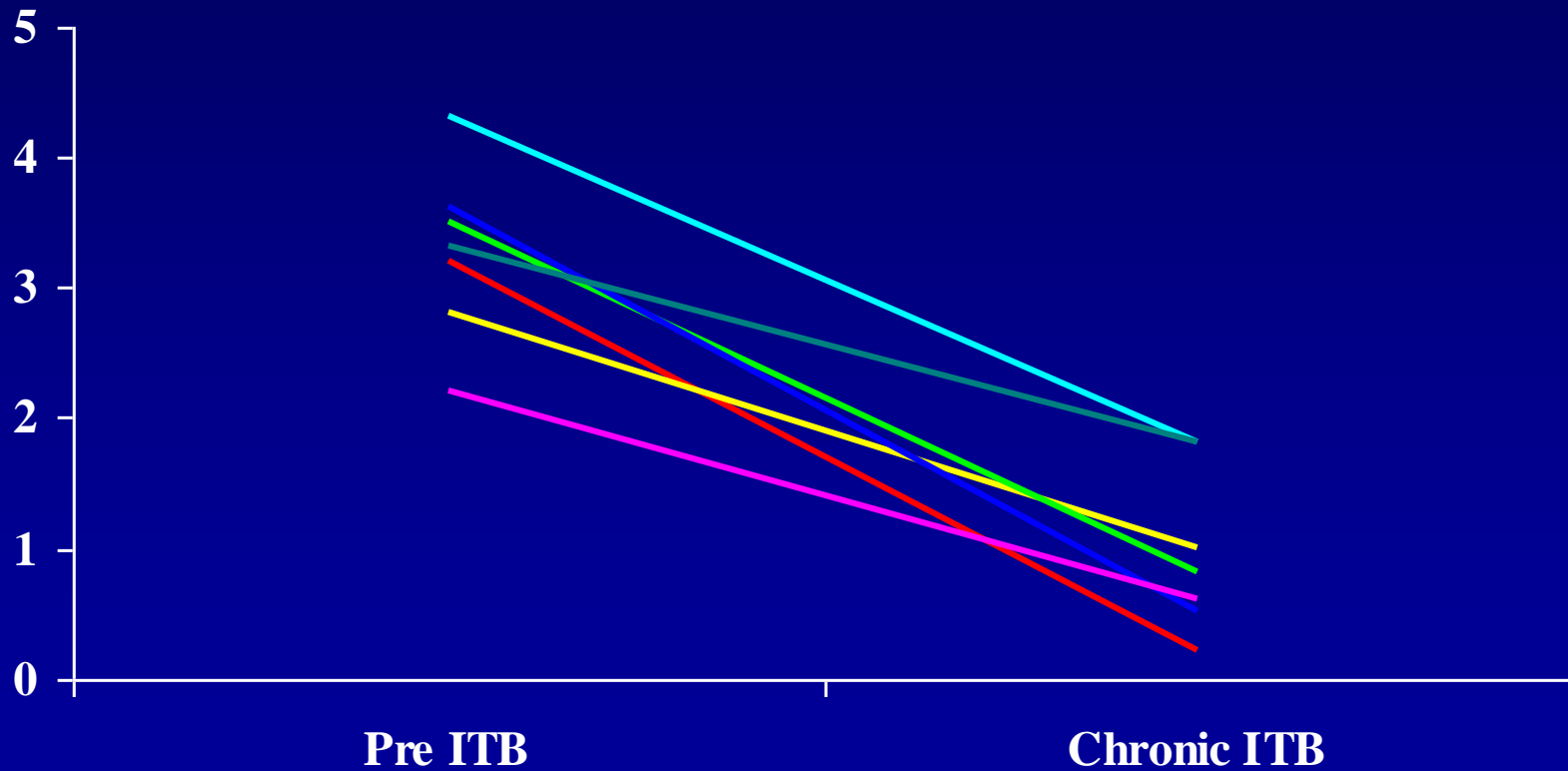
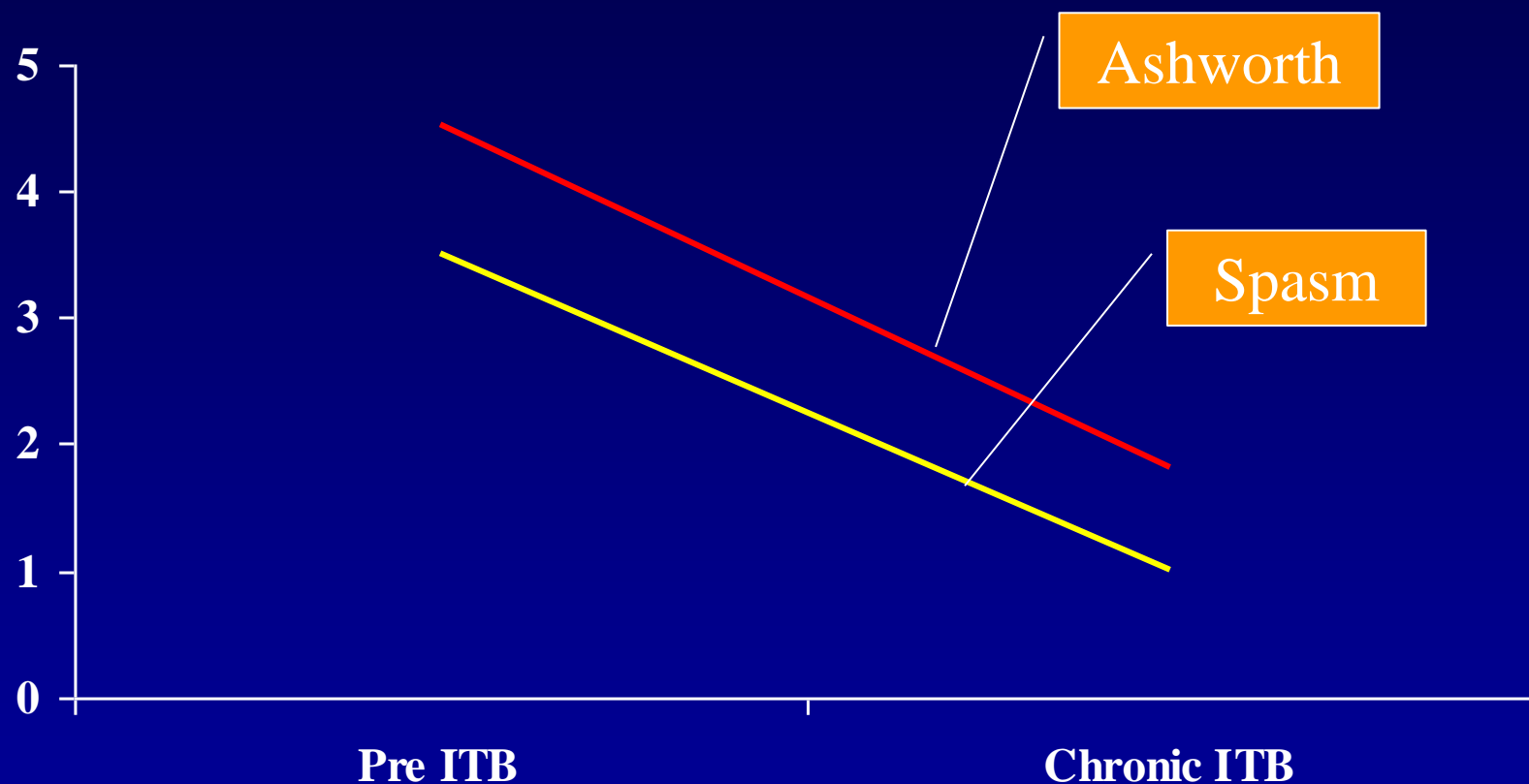
- scala di Ashworth
- scala di Penn
- scale funzionali
- tests neurofisiologici

# INTRATHECAL BACLOFEN FOR SPINAL SPASTICITY

5
4
3
2
1
0

Pre ITB

Chronic ITB

# INTRATHECAL BACLOFEN FOR SPINAL SPASTICITY

Neurochirurgia UCSC Roma

# Intrathecal baclofen for spinal spasticity

| | Pre ITB | Chronic ITB |
|---|---|---|
| Mean Asworth score : | 4,5 +/- 0,7 | 1,8 +/- 0,5 |
| Mean Spasm score : | 3,5 +/- 0,3 | 1 +/- 0,5 |

# INTRATHECAL BACLOFEN FOR CEREBRAL SPASTICITY
# 1991 - 2001 LITERATURE

- NARAYAN, NEUROL, 1991*
- ALBRIGHT, JAMA, 1993
- PENN, MOV DISORD, 1995*
- ARMSTRONG, J NEUROSURG, 1997
- GERSZTEN, PED NEUROSURG, 1997
- GERSZTEN, J NEUROSURG, 1998
- WALKER, MOV DISORD, 2000*
- VAN SCHAEJBROEUCK, NEUROSURG, 2000
- MEYTHALER, ARCH PHYS MED REHABIL, 2001

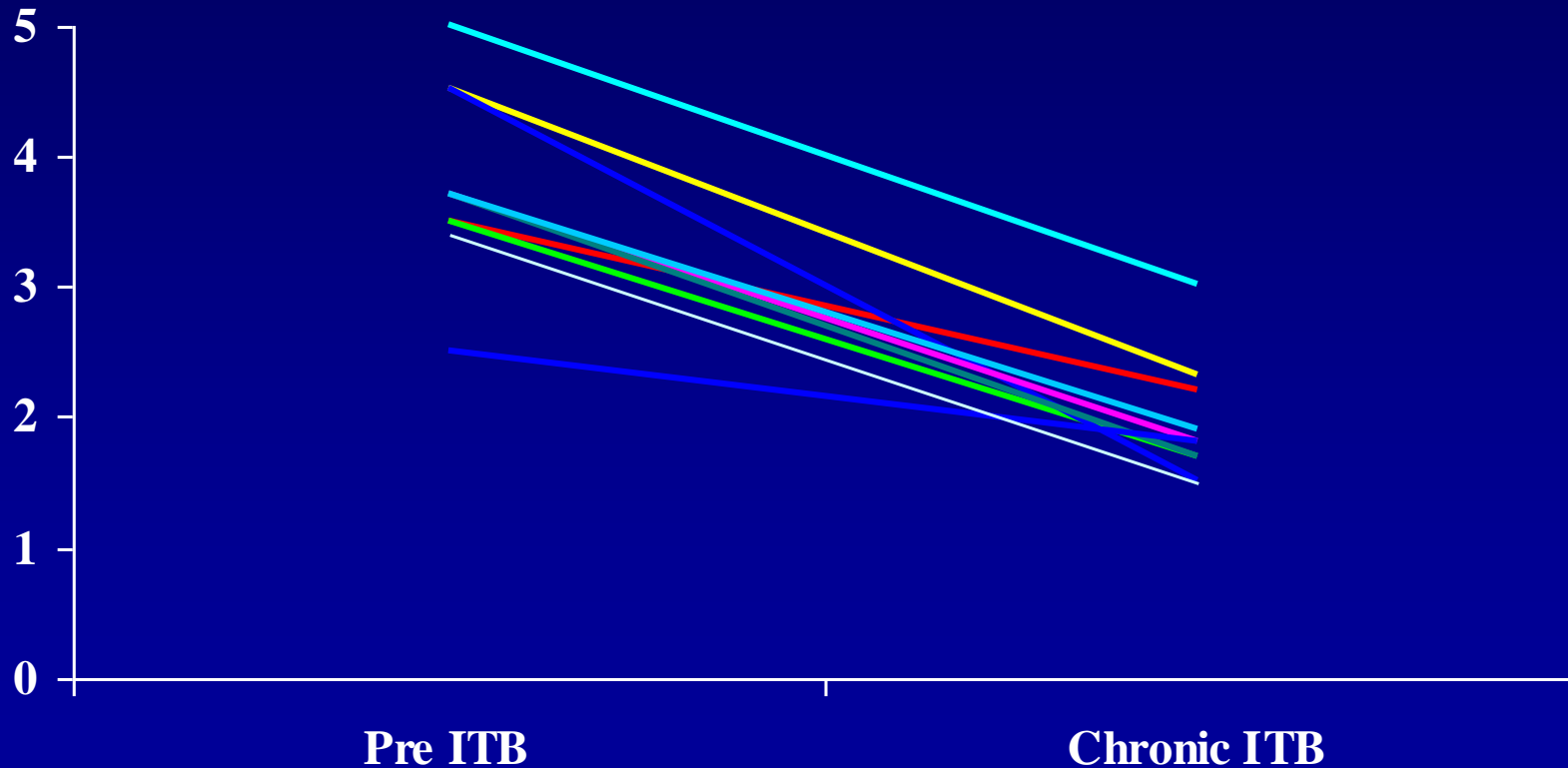
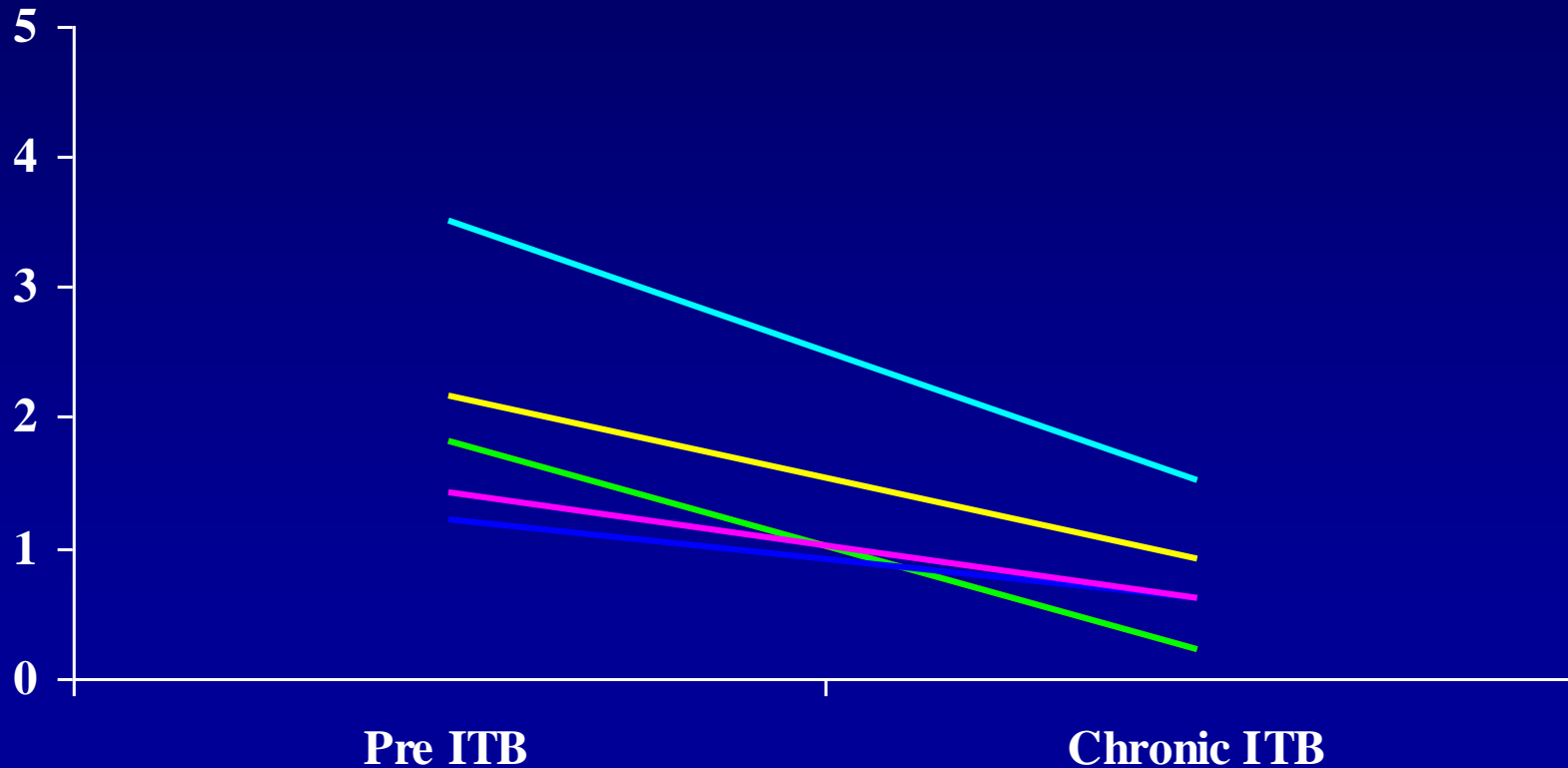
*** Dystonia**

## INTRATHECAL BACLOFEN FOR CEREBRAL SPASTICITY
## 1991 - 2001 LITERATURE

**170 PATIENTS**

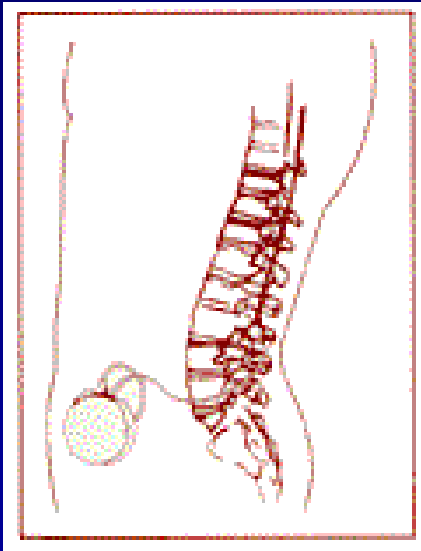
**MEAN FOLLOW-UP : 12-72 months**

**MEAN DAILY DOSE : 200-825 ug**

# INTRATHECAL BACLOFEN FOR CEREBRAL SPASTICITY

# INTRATHECAL BACLOFEN FOR CEREBRAL SPASTICITY

# INTRATHECAL BACLOFEN FOR SPASTICITY DUE TO TRAUMATIC OR HYPOXIC BRAIN INJURY LITERATURE

- MEYTHALER, J NEUROSURG, 1999
- BECKER, J NEUROL, 1997
- MEYTHALER, ARCH PHYS MED REHABIL, 1999
- RAWICKI, J NEUROSURG, 1999
- FRANÇOIS, J TRAUMA, 2001

# Intrathecal Baclofen infusion in severe spasticity due to acquired brain injury

## CLINICAL EVALUATION

- Ashworth scale for hypertonia
- Penn scale for painful spasms
- Neurovegetative storms
- Functional assessment
- Adverse events

# Intrathecal Baclofen infusion in severe spasticity due to acquired brain injury

## CONTINUOUS INFUSION

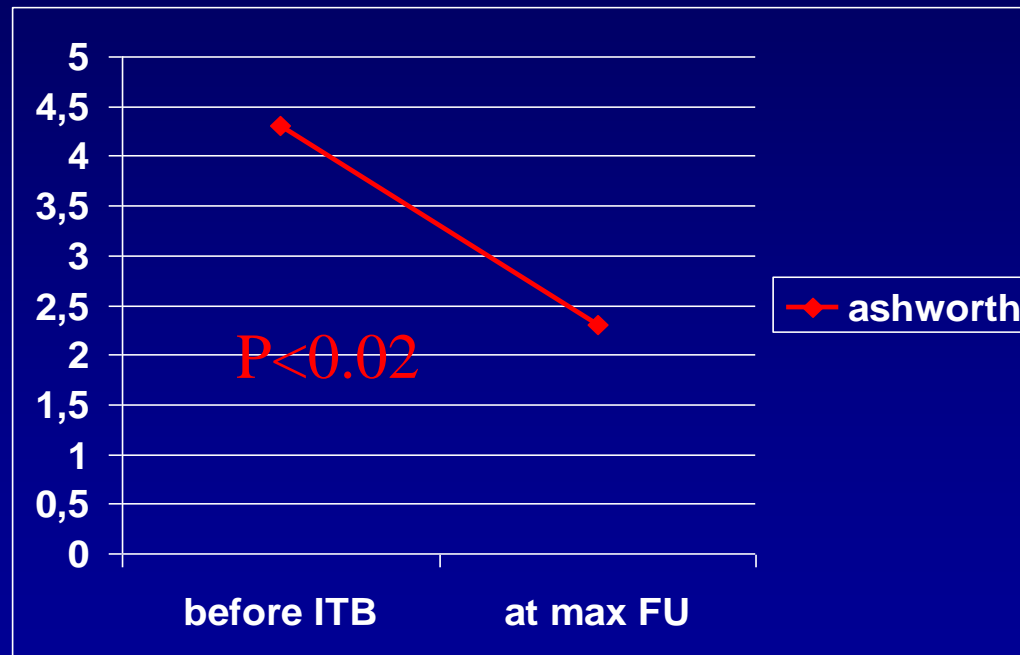
**Initial mean daily dose: 137.8+/-117ug**

**min: 50ug; max: 150ug**

**Mean daily dose at max FU: 222.5+/-203ug**

**min: 50ug; max: 740ug**

# Intrathecal Baclofen infusion in severe spasticity due to acquired brain injury

## Results on muscle hypertonus: Ashworth scale

**In 8 cases no difference between effect at upper and lower extremities**

# Intrathecal Baclofen infusion in severe spasticity due to acquired brain injury

## Results on painful spasms: 6 patients

- Disappeared in 5 cases
- Decreased in 1 case

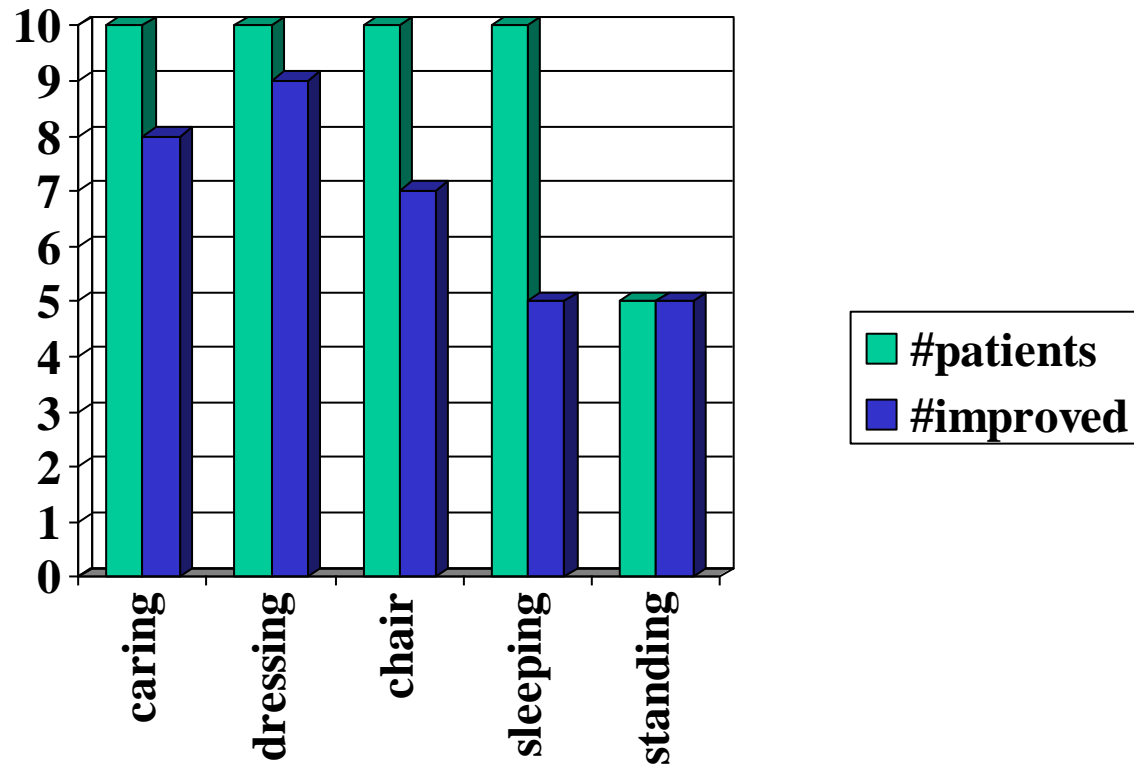
## Results on vegetative storms: 4 patients

- Disappeared in 3 cases
- Decreased in 1 case

# Intrathecal Baclofen infusion in severe spasticity due to acquired brain injury

## Functions of daily life: results

10
9
8
7
6
5
4
3
2
1
0

caring
dressing
chair
sleeping
standing

#patients
#improved

# BACLOFEN INTRATECALE

## quali pazienti possono beneficiare del trattamento ?

95% of the patients respond to intrathecal Baclofen

90% of the patients continue to receive intrathecal Baclofen at long term

**R. Penn, 2000**

# BACLOFEN
## GABA-B agonista

Deprime i riflessi mono e polisinaptici:

**diminuisce ipertono e spasmi**

**non migliora la paralisi**

# BACLOFEN INTRATECALE
## Obiettivi raggiungibili

- diminuzione ipertono e spasmi
- miglioramento del riposo notturno
- facilitazione di cure personali, trasferimenti, mantenimento della posizione seduta, utilizzo degli arti superiori
- minore dipendenza da terzi

# BACLOFEN INTRATECALE
# Conclusioni

- Baclofen è un potente antispastico, diminuisce ipertono e spasmi, non cura la paralisi
- Miglior selezione: bolo test
- Importanza collaborazione tra paziente, riabilitatore, famiglia, medico di base per ottimizzare i risultati e avere miglioramenti funzionali
- Importanza di un sistema d'infusione affidabile e duttile

# Neurochirurgia Funzionale

- dolore
- spasticità
- epilessia
- malattia di Parkinson
- distonie
- altri disturbi del movimento
- disturbi della personalità
- cefalee
- ….